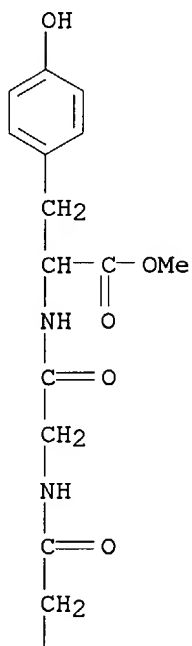


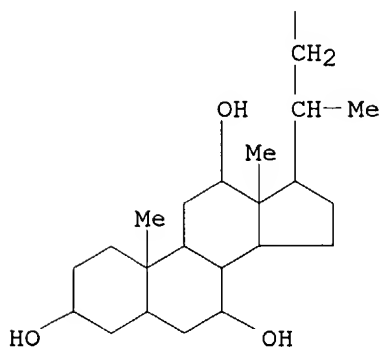
10/088807

INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, L-tyrosine deriv.  
MF C36 H54 N2 O8  
LC STN Files: CA, CAPLUS, TOXCENTER  
DT.CA Caplus document type: Patent  
RL.P Roles from patents: ANST (Analytical study)

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

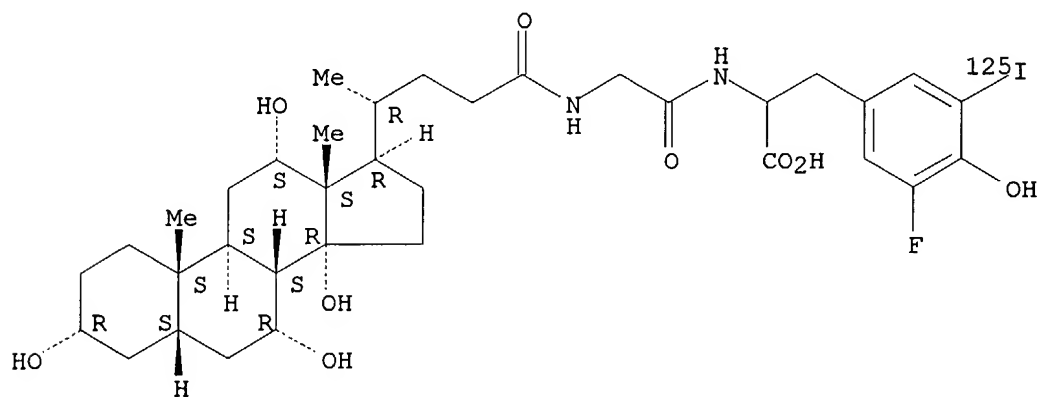
10/088807

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 93:65429

L22 ANSWER 86 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 69889-03-8 REGISTRY  
CN Tyrosine, 3-fluoro-5-(iodo-125I)-N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12,14-tetrahydroxy-24-oxocholan-24-yl]glycyl]- (9CI)  
(CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, tyrosine deriv.  
FS STEREOSEARCH  
MF C35 H50 F I N2 O9  
LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 90:168979

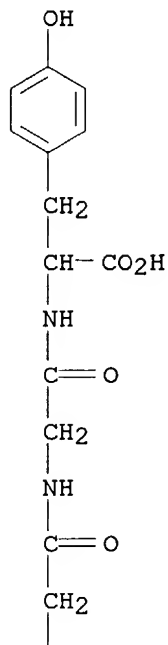
L22 ANSWER 89 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 67319-56-6 REGISTRY  
CN L-Tyrosine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]glycyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, L-tyrosine deriv.  
MF C35 H52 N2 O8  
CI COM  
LC STN Files: CA, CAPLUS, MEDLINE, TOXCENTER, USPATFULL  
DT.CA CAplus document type: Journal; Patent  
RL.P Roles from patents: PREP (Preparation); RACT (Reactant or reagent)  
RLD.P Roles for non-specific derivatives from patents: PREP (Preparation)  
RL.NP Roles from non-patents: BIOL (Biological study); PREP

Searcher : Shears 571-272-2528

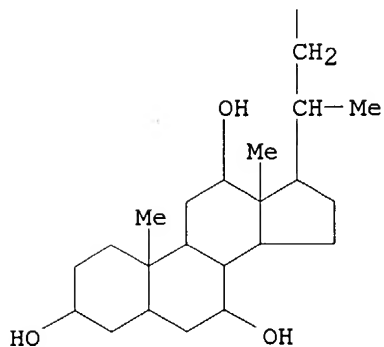
10/088807

(Preparation); PROC (Process)  
RLD.NP Roles for non-specific derivatives from non-patents: BIOL  
(Biological study)

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

9 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
9 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Searcher : Shears 571-272-2528

REFERENCE 1: 117:23700  
 REFERENCE 2: 110:185790  
 REFERENCE 3: 108:19604  
 REFERENCE 4: 105:76527  
 REFERENCE 5: 100:100527  
 REFERENCE 6: 94:103833  
 REFERENCE 7: 93:155866  
 REFERENCE 8: 92:142864  
 REFERENCE 9: 89:103269

L22 ANSWER 90 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **61761-30-6** REGISTRY

CN L-Lysinamide, N2-[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-N6-[(phenylmethoxy)carbonyl]-L-lysyl-N6-[(phenylmethoxy)carbonyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, L-lysineamide deriv.

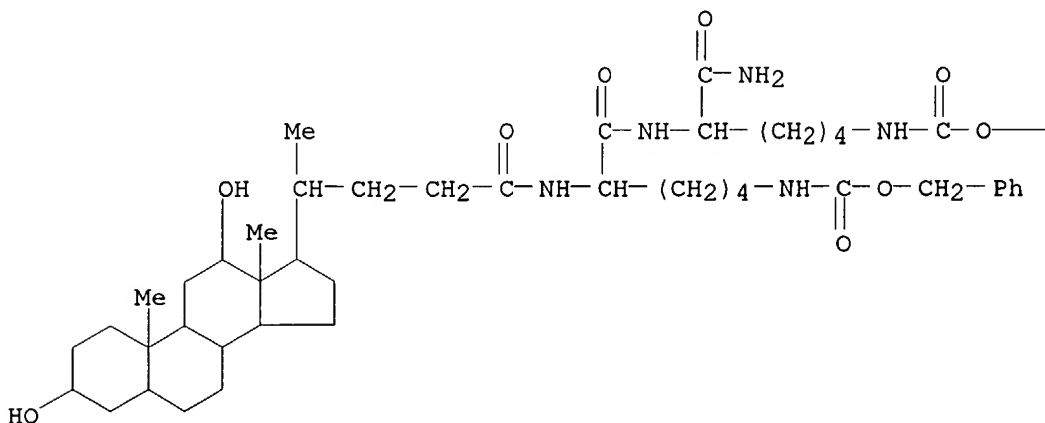
MF C52 H77 N5 O9

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

PAGE 1-A



—CH<sub>2</sub>—Ph

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 86:73105

L22 ANSWER 91 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **61734-77-8** REGISTRYCN L-Lysinamide, N2-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-lysyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

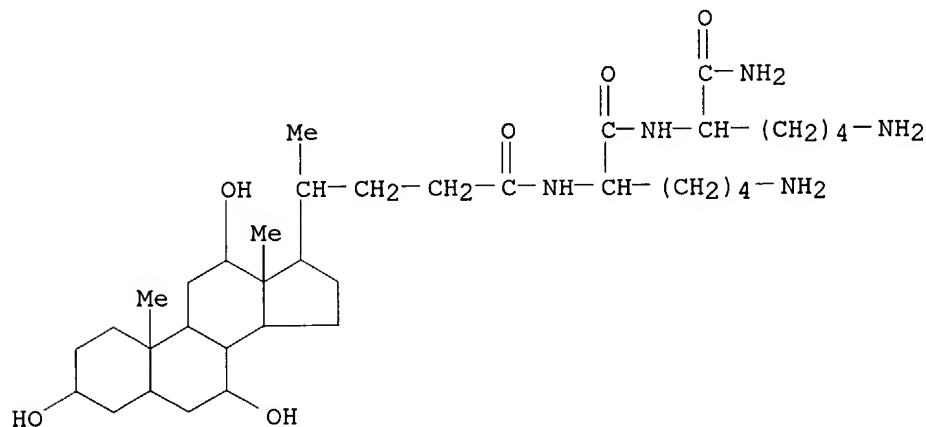
CN Cholane, lysinamide deriv.

MF C36 H65 N5 O6

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 86:73104

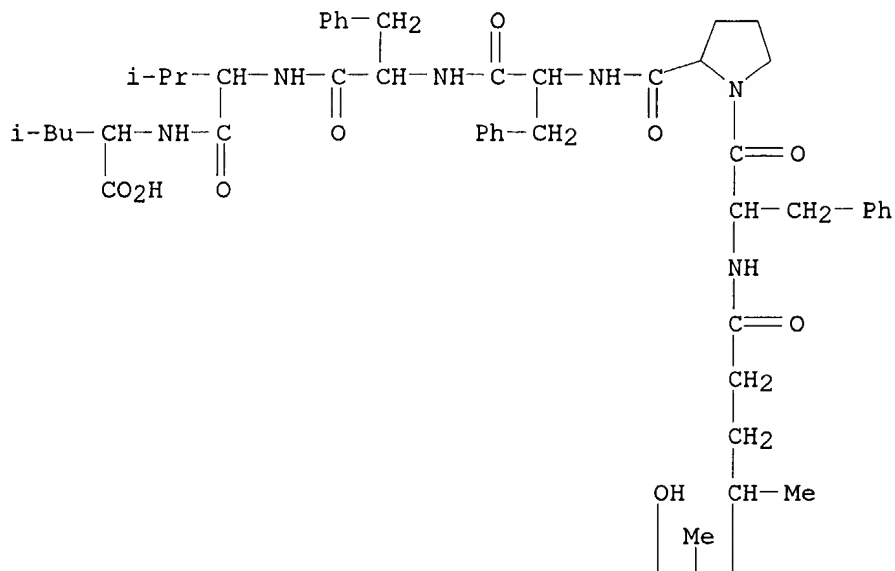
L22 ANSWER 94 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **60667-86-9** REGISTRYCN D-Leucine, N-[N-[N-[N-[1-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-D-phenylalanyl]-L-prolyl]-L-

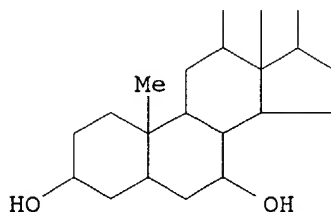
phenylalanyl]-L-phenylalanyl]-L-valyl]- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Cholane, D-leucine deriv.  
 FS PROTEIN SEQUENCE  
 MF C67 H94 N6 O11  
 LC STN Files: CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, USPATFULL  
 DT.CA CAPLUS document type: Patent  
 RL.P Roles from patents: PREP (Preparation)

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 85:143523

10/088807

L22 ANSWER 95 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **39830-10-9** REGISTRY

CN Griselimycin, 1-de(N-acetyl-N-methyl-L-valine)-2-[trans-4-methyl-1-  
[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-  
oxocholan-24-yl]-L-proline]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 1H,12H-Dipyrrolo[2,1-i:2',1'-r][1,4,7,10,13,16,19,22]oxaheptaazacycl  
opentacosine, cyclic peptide deriv.

CN Cholane, griselimycin deriv.

FS PROTEIN SEQUENCE

MF C73 H121 N9 O14

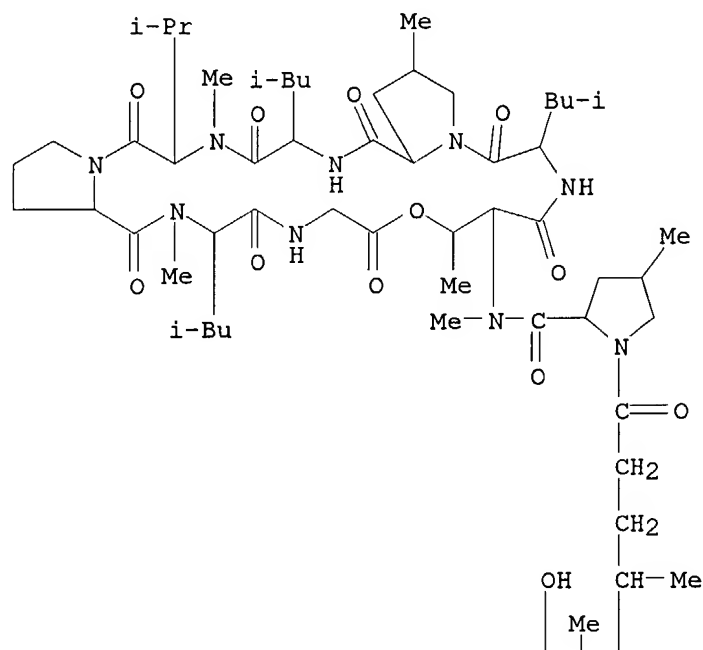
LC STN Files: CA, CAPLUS

DT.CA CAPLUS document type: Patent

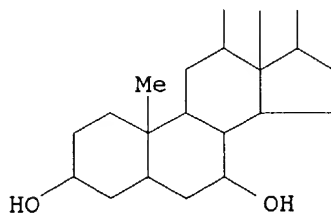
RL.P Roles from patents: PREP (Preparation)

**\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\***

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10/088807

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 78:84820

L22 ANSWER 96 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 26563-58-6 REGISTRY

CN Glycine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]glycyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, glycine deriv.

CN Glycine, N-(N-choloylglycyl)- (8CI)

OTHER NAMES:

CN Cholyldiglycine

CN Glycylglycocholic acid

FS STEREOSEARCH

MF C28 H46 N2 O7

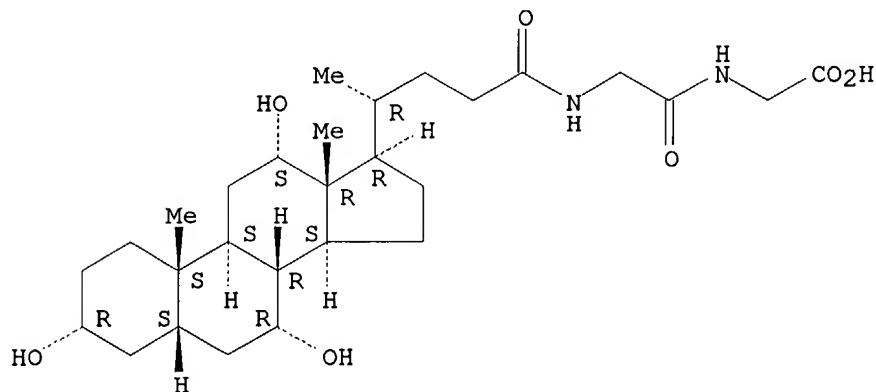
CI COM

LC STN Files: CA, CAPLUS

DT.CA CAPLUS document type: Journal

RL.NP Roles from non-patents: ANST (Analytical study); PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1907 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:210476

REFERENCE 2: 105:76527

REFERENCE 3: 104:183781

Searcher : Shears 571-272-2528

10/088807

REFERENCE 4: 104:45877

REFERENCE 5: 72:86455

L22 ANSWER 97 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **22154-47-8** REGISTRY

CN Glycine, N-[N-[N-[N-[N-(N-choloylglycyl)glycyl]glycyl]glycyl]glycyl]-  
(8CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C36 H58 N6 O11

LC STN Files: CA, CAPLUS

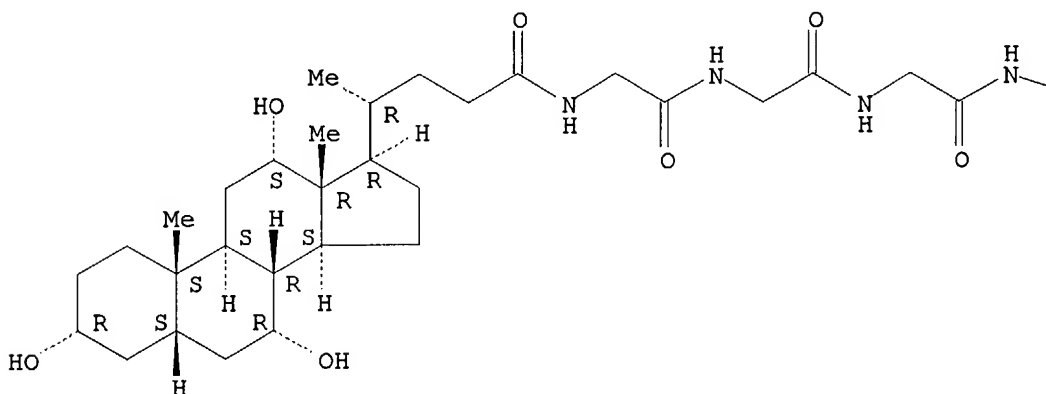
DT.CA CAPLUS document type: Journal

RL.NP Roles from non-patents: PROC (Process)

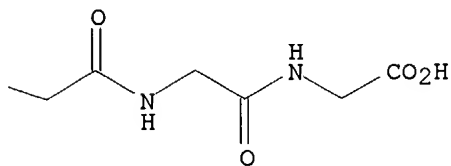
\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 70:2361

L22 ANSWER 98 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **5163-93-9** REGISTRY

CN Butyric acid, 4,4'-dithiobis[2-(3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -  
trihydroxy-5 $\beta$ -cholanamido)- (7CI, 8CI) (CA INDEX NAME)

MF C56 H92 N2 O12 S2

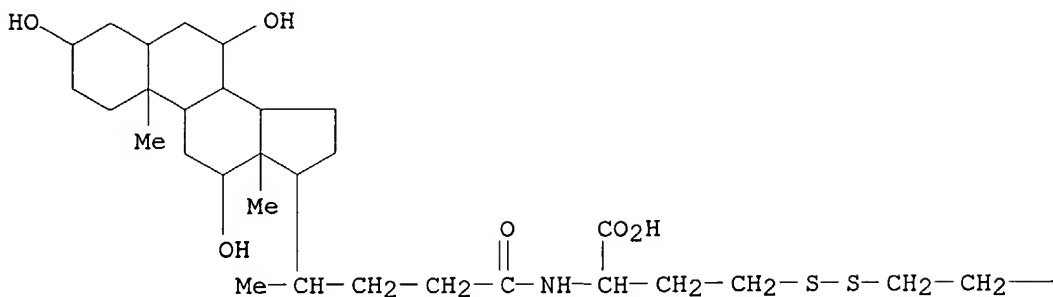
LC STN Files: CA, CAOLD, CAPLUS

Searcher : Shears 571-272-2528

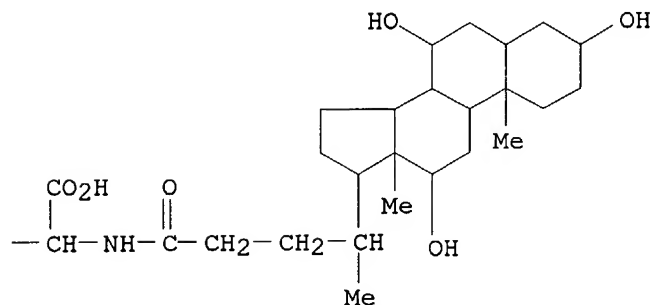
10/088807

DT.CA CAplus document type: Journal  
RL.NP Roles from non-patents: NORL (No role in record)

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1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 63:100804

FILE 'CAOLD' ENTERED AT 12:24:55 ON 28 JUL 2004  
L23 1 S L22

L23 ANSWER 1 OF 1 CAOLD COPYRIGHT 2004 ACS on STN

AN CA63:18614h CAOLD

TI protection from ionizing radiation - (IV) influence of Na  
cysteinethiosulfonate on the results of x-ray treatment of  
transplantable Crocker sarcoma

AU Zebro, Tadeusz; Jorasz, E.; Szczepkowski, T. W.; Stachura, J.;  
Niezabitowski, A.

TI radioprotective agents-substituted amides of cholic acid

AU Crippa, Giunio B.; Bellini, A. M.; Crippa, A.; Rondanelli, E. G.

IT 56-10-0 2365-14-2 2545-31-5 5163-91-7 5163-93-9  
5169-54-0 107660-12-8

Searcher : Shears 571-272-2528

10/088807

FILE 'USPATFULL' ENTERED AT 12:25:19 ON 28 JUL 2004

L24 12 S L22

L25 11 S L24 NOT (PY=>1999 OR PD=>19990730)

L25 ANSWER 1 OF 11 USPATFULL on STN

ACCESSION NUMBER: 1998:108384 USPATFULL

TITLE: Lipid conjugates of therapeutic peptides and protease inhibitors

INVENTOR(S): Basava, Channa, San Diego, CA, United States  
Hostetler, Karl Y., Del Mar, CA, United States

PATENT ASSIGNEE(S): NeXstar Pharmaceuticals, Inc., Boulder, CO,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5804552		19980908
APPLICATION INFO.:	US 1995-458401		19950602 (8)
RELATED APPLN. INFO.:	Division of Ser. No. US 1991-734434, filed on 23 Jul 1991, now patented, Pat. No. US 5554728		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Tsang, Cecilia J.		
ASSISTANT EXAMINER:	Lukton, David		
LEGAL REPRESENTATIVE:	Swanson & Bratschun, L.L.C.		
NUMBER OF CLAIMS:	5		
EXEMPLARY CLAIM:	1,2		
LINE COUNT:	1301		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds wherein therapeutic peptides, including HIV protease inhibitors, are covalently linked to phospholipids, glycerides or other membrane-targeting and membrane-anchoring species, and their pharmaceutically acceptable salts, together with processes for their preparation. The invention also provides novel HIV protease inhibitors. The compounds of the present invention possess useful pharmacological properties such as antiviral activity towards viral infection and inhibitory activity towards viral proteases. Therefore, these compounds can be used in the prophylaxis or treatment of viral infections, in particular infections caused by HIV and other retroviruses. The targeting technology as described for the protease inhibitors is also applicable to a variety of inhibitors of other enzymes.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 2 OF 11 USPATFULL on STN

ACCESSION NUMBER: 97:59371 USPATFULL

TITLE: Bile acid inhibitors of metalloproteinase enzymes

INVENTOR(S): Jacobson, Alan R., Somerville, MA, United States  
Gabler, Douglas G., Cambridge, MA, United States  
Oleksyszyn, Jozef, Arlington, MA, United States

PATENT ASSIGNEE(S): OsteoArthritis Sciences, Inc., Cambridge, MA,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5646316		19970708

Searcher : Shears 571-272-2528

10/088807

APPLICATION INFO.: US 1995-430129 19950425 (8)  
RELATED APPLN. INFO.: Continuation of Ser. No. US 1994-224427, filed on  
8 Apr 1994, now abandoned  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Cook, Rebecca  
LEGAL REPRESENTATIVE: Hamilton, Brook, Smith & Reynolds, P.C.  
NUMBER OF CLAIMS: 5  
EXEMPLARY CLAIM: 1  
LINE COUNT: 911

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention relates to a bile acid derivative, which comprises a bile acid derivatized at the carboxyl group with a hydroxamic acid or hydroxamate ester. The carboxyl group in the bile acid compound can also be derivatized with an amino acid or oligopeptide, whose C-terminus is derivatized with a hydroxamic acid or a hydroxamate ester. The present invention also relates to a method of use of a bile acid or a bile acid derivative to inhibit a metalloproteinase enzyme, comprising contacting a metalloproteinase with an effective amount of a bile acid or bile acid derivative. In another embodiment, the present invention further relates to a method of use of a bile acid or bile acid derivative to therapeutically treat a disease, which is ameliorated by inhibiting a metalloproteinase enzyme. In this method, a therapeutically effective amount of a bile acid, a bile acid derivative or physiologically acceptable salts thereof, is administered to a human or other mammal.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 3 OF 11 USPATFULL on STN  
ACCESSION NUMBER: 96:82799 USPATFULL  
TITLE: Lipid conjugates of therapeutic peptides and  
protease inhibitors  
INVENTOR(S): Basava, Channa, San Diego, CA, United States  
Hostetler, Karl Y., Del Mar, CA, United States  
PATENT ASSIGNEE(S): NeXstar Pharmaceuticals, Inc., Boulder, CO,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5554728		19960910
APPLICATION INFO.:	US 1991-734434		19910723 (7)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Scheiner, Toni R.		
ASSISTANT EXAMINER:	Huff, Sheela J.		
LEGAL REPRESENTATIVE:	Swanson & Bratschun, LLC		
NUMBER OF CLAIMS:	8		
EXEMPLARY CLAIM:	1		
LINE COUNT:	1829		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Compounds wherein therapeutic peptides are covalently linked to phospholipids, glycerides or other membrane-targeting and membrane-anchoring species, and their pharmaceutically acceptable salts, together with processes for their preparation. The

Searcher : Shears 571-272-2528

10/088807

targeting technology is applicable to HIV protease inhibitors and a variety of other enzyme inhibitors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 4 OF 11 USPATFULL on STN  
ACCESSION NUMBER: 95:78165 USPATFULL  
TITLE: Potent non-opiate analgesic  
INVENTOR(S): Ruff, Michael R., Potomac, MD, United States  
Hill, Joanna M., Gaithersburg, MD, United States  
Kwart, Lawrence D., Germantown, MD, United States  
Pert, Candace B., Potomac, MD, United States  
PATENT ASSIGNEE(S): Advanced Peptides & Biotechnology Sciences,  
Sewickley, PA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 5446026		19950829
APPLICATION INFO.:	US 1993-19830		19930219 (8)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 1992-850141, filed on 12 Mar 1992, now abandoned which is a continuation of Ser. No. US 1990-541199, filed on 11 Jun 1990, now abandoned which is a continuation of Ser. No. US 1989-391272, filed on 9 Aug 1989, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Lee, Lester L.		
LEGAL REPRESENTATIVE:	Cobrin Gittes & Samuel		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	10 Drawing Figure(s); 7 Drawing Page(s)		
LINE COUNT:	155		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to Cholic, Chenodeoxycholic and deoxycholic acid derivatives of a peptide having the sequence:  
Pro-Arg-Thr-Asn-Thr-Gly-Ser-Gly-Thr-Pro-amide and use thereof in inducing analgesia.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 5 OF 11 USPATFULL on STN  
ACCESSION NUMBER: 89:17024 USPATFULL  
TITLE: Bile acid derivatives, their salts and production thereof  
INVENTOR(S): Hatono, Shunsou, Koda, Japan  
Yazaki, Akira, Koda, Japan  
Yokomoto, Masaharu, Koda, Japan  
Hirao, Yuzo, Koda, Japan  
PATENT ASSIGNEE(S): Wakunaga Seiyaku Kabushiki Kaisha, Osaka, Japan  
(non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4810422		19890307
APPLICATION INFO.:	US 1987-91957		19870901 (7)

Searcher : Shears 571-272-2528

10/088807

	NUMBER	DATE
PRIORITY INFORMATION:	JP 1986-208901	19860905
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	Granted	
PRIMARY EXAMINER:	Schenkman, Leonard	
ASSISTANT EXAMINER:	Lipovsky, Joseph A.	
LEGAL REPRESENTATIVE:	Wenderoth, Lind & Ponack	
NUMBER OF CLAIMS:	4	
EXEMPLARY CLAIM:	1	
LINE COUNT:	984	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A bile acid derivative of the following formula (I): ##STR1## wherein: X is a halogen atom; R.sub.1 is a hydrogen atom or a lower alkyl group; Y is ##STR2## (wherein n is an integer of from 0 to 5); each of R.sub.2 and R.sub.3 is a hydrogen atom or a hydroxyl group; R.sub.4 is a hydroxyl group, lower alkoxy group, ##STR3## (wherein R.sub.5 is a hydrogen atom or a lower alkoxy group, R.sub.6 is a carboxyl group, benzyloxycarbonyl group or sulfonyl group, or a salt thereof, and m is an integer of from 1 to 4); the intermittent line, . . . , is an  $\alpha$ -bond; and the wavy line, , is an  $\alpha$ - or  $\beta$ -bond, and a salt thereof, and a process for production thereof.

This bile acid derivative has carcinostatic activity and yet is of low toxicity. Accordingly, this compound can be used as a carcinostatic agent.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 6 OF 11 USPATFULL on STN

ACCESSION NUMBER: 82:2231 USPATFULL  
TITLE: Monoradioiodinated imidazole derivatives  
INVENTOR(S): Akerkar, Anandrao S., Pomona, NY, United States  
Rutner, Herman, Hackensack, NJ, United States  
PATENT ASSIGNEE(S): Becton Dickinson & Company, Paramus, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4310675		19820112
APPLICATION INFO.:	US 1979-42009		19790524 (6)
RELATED APPLN. INFO.:	Division of Ser. No. US 1978-885447, filed on 10 Mar 1978, now patented, Pat. No. US 4202874 which is a division of Ser. No. US 1976-727407, filed on 29 Sep 1976, now patented, Pat. No. US 4120867		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Schwartz, Richard A.		
LEGAL REPRESENTATIVE:	Marn, Louis E., Olstein, Elliot M.		
NUMBER OF CLAIMS:	11		
EXEMPLARY CLAIM:	1		
LINE COUNT:	493		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Monoradioiodinated derivatives of compounds employed in a

Searcher : Shears 571-272-2528

10/088807

radioassay prepared from precursors which are either active esters, amino acids, or amines, including a phenolic of imidazole substituent group in which one of the possible two sites on the group for radioiodination is substituted to permit production of a monoradioiodinated derivative. A preferred precursor is an active ester of 3-fluoro-5-radioiodotyrosine which can be coupled to a compound including an amino group to produce a monoradioiodinated derivative of the compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 7 OF 11 USPATFULL on STN

ACCESSION NUMBER: 80:42971 USPATFULL

TITLE: Method and reagents for measuring the level of conjugated bile acids

INVENTOR(S): Hixson, Jr., Harry F., Libertyville, IL, United States

Green, Billy J., Vernon Hills, IL, United States

Cummins, Laurence M., Libertyville, IL, United States

States

Cole, John W., Deerfield, IL, United States

PATENT ASSIGNEE(S): Abbott Laboratories, North Chicago, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4220598		19800902
APPLICATION INFO.:	US 1977-851095		19771114 (5)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1976-677586, filed on 16 Apr 1976, now abandoned		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Roberts, Elbert L.		
LEGAL REPRESENTATIVE:	Willmann, Neal O.		
NUMBER OF CLAIMS:	2		
EXEMPLARY CLAIM:	1,2		
LINE COUNT:	264		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method and novel reagents useful for measuring the level of specific immunoreactive conjugated bile acids in a sample using labeled conjugated bile acid derivatives are disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 8 OF 11 USPATFULL on STN

ACCESSION NUMBER: 80:28203 USPATFULL

TITLE: Process for purifying iodinated bile acid conjugates

INVENTOR(S): Spenney, Jerry G., Birmingham, AL, United States

PATENT ASSIGNEE(S): The United States of America as represented by the Administrator of Veterans Affairs, Washington, DC, United States (U.S. government)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4207308		19800610

Searcher : Shears 571-272-2528

10/088807

APPLICATION INFO.: US 1977-805960 19770613 (5)  
RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 1976-719753,  
filed on 2 Sep 1976, now abandoned  
DOCUMENT TYPE: Utility  
FILE SEGMENT: Granted  
PRIMARY EXAMINER: Padgett, Benjamin R.  
ASSISTANT EXAMINER: Nucker, Christine M.  
LEGAL REPRESENTATIVE: Zitver, Leon, Latker, Norman J., Ferris, Thomas  
G.  
NUMBER OF CLAIMS: 19  
EXEMPLARY CLAIM: 1  
NUMBER OF DRAWINGS: 10 Drawing Figure(s); 6 Drawing Page(s)  
LINE COUNT: 802

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Iodinatable bile salt derivatives are obtained by providing bile salts and their glycine and taurine conjugates with iodinated groups. The radioiodinated compounds are useful in the radioimmunoassay of bile salts and in physiological studies. The preferred compound is cholyglycylhistamine. The synthesis of radioiodinated conjugates and their purification by extraction and silica gel chromatography are described.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 9 OF 11 USPATFULL on STN

ACCESSION NUMBER: 80:23335 USPATFULL  
TITLE: Monoradioiodinated derivatives and precursors for production thereon  
INVENTOR(S): Akerkar, Anandrao S., Pomona, NY, United States  
Rutner, Herman, Hackensack, NJ, United States  
PATENT ASSIGNEE(S): Becton Dickinson & Company, Paramus, NJ, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4202874		19800513
APPLICATION INFO.:	US 1978-885447		19780310 (5)
RELATED APPLN. INFO.:	Division of Ser. No. US 1976-727407, filed on 29 Sep 1976, now patented, Pat. No. US 4120867		
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Padgett, Benjamin R.		
ASSISTANT EXAMINER:	Nucker, Christine M.		
LEGAL REPRESENTATIVE:	Marn, Louis E., Olstein, Elliot M.		
NUMBER OF CLAIMS:	17		
EXEMPLARY CLAIM:	1,17		
LINE COUNT:	485		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Monoradioiodinated derivatives of compounds employed in a radioassay prepared from precursors which are either active esters, amino acids, or amines, including a phenolic or imidazole substituent group in which one of the possible two sites on the group for radioiodination is substituted to permit production of a monoradioiodinated derivative. A preferred precursor is an active ester of 3-fluoro-5-radioiodotyrosine which can be coupled to a compound including an amino group to produce a monoradioiodinated

10/088807

derivative of the compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 10 OF 11 USPATFULL on STN  
ACCESSION NUMBER: 78:58684 USPATFULL  
TITLE: Monoradioiodinated phenolic esters, acids and amines  
INVENTOR(S): Akerkar, Anandrao S., Pomona, NY, United States  
Rutner, Herman, Hackensack, NJ, United States  
PATENT ASSIGNEE(S): Becton, Dickinson & Company, Rutherford, NJ,  
United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 4120867		19781017
APPLICATION INFO.:	US 1976-727407		19760929 (5)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Tovar, Jose		
LEGAL REPRESENTATIVE:	Marn & Jangarathis		
NUMBER OF CLAIMS:	18		
EXEMPLARY CLAIM:	1		
LINE COUNT:	483		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Monoradioiodinated derivatives of compounds employed in a radioassay prepared from precursors which are either active esters, amino acids, or amines, including a phenolic or imidazole substituent group in which one of the possible two sites on the group for radioiodination is substituted to permit production of a monoradioiodinated derivative. A preferred precursor is an active ester of 3-fluoro-5-radioidotyrosine which can be coupled to a compound including an amino group to produce a monoradioiodinated derivative of the compound.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L25 ANSWER 11 OF 11 USPATFULL on STN  
ACCESSION NUMBER: 76:41685 USPATFULL  
TITLE: Cathepsin in D inhibitors  
INVENTOR(S): Wagner, Arthur F., Princeton, NJ, United States  
Holly, Frederick W., Glenside, PA, United States  
Lin, Tsau-Yen, Piscataway, NJ, United States  
Shen, Tsung-Ying, Westfield, NJ, United States  
Hirschmann, Ralph F., Blue Bell, PA, United States  
PATENT ASSIGNEE(S): Merck & Co., Inc., Rahway, NJ, United States  
(U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 3971736		19760727
APPLICATION INFO.:	US 1975-542884		19750121 (5)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	Granted		
PRIMARY EXAMINER:	Gotts, Lewis		

Searcher : Shears 571-272-2528

10/088807

ASSISTANT EXAMINER: Suyat, Reginald J.  
LEGAL REPRESENTATIVE: Monaco, Mario A., Westlake, Jr., Harry E.  
NUMBER OF CLAIMS: 10  
EXEMPLARY CLAIM: 1  
LINE COUNT: 758

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Hexa- and heptapeptides of formula W-[X-Pro-Phe-Phe-Y-Z].sub.n H prepared by standard synthetic peptide techniques are anti-inflammatory, anti-rheumatoid arthritic and anti-ulcer agents.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

(FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 12:26:19 ON 28 JUL 2004)

L26 7 S L22

L27 7 DUP REM L26 (0 DUPLICATES REMOVED)

L27 ANSWER 1 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 92234471 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 1314773  
TITLE: Characterization of the transport of a synthetic bile salt, iodinated cholyl-glycyl-tyrosine, in isolated cultured rat hepatocytes.  
AUTHOR: Deutsch J C; Iwahashi M M; Sutherland E M; Mapoles J; Simon F R  
CORPORATE SOURCE: Hepatobiliary Research Center, University of Colorado School of Medicine, Denver.  
CONTRACT NUMBER: DK-15851 (NIDDK)  
DK-34914 (NIDDK)  
SOURCE: Hepatology (Baltimore, Md.), (1992 May) 15 (5) 917-22.  
Journal code: 8302946. ISSN: 0270-9139.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 199205  
ENTRY DATE: Entered STN: 19920612  
Last Updated on STN: 19920612  
Entered Medline: 19920526

AB The uptake of tri-hydroxy conjugated bile salts by hepatocytes is principally by a sodium-dependent carrier. We examined the uptake kinetics of the high-specific-activity, hydroxylated, conjugated bile salt 125I-labeled cholyl-glycyl-tyrosine, to determine whether this synthetic bile salt was transported by the sodium-dependent bile salt system. 125I-labeled cholyl-glycyl-tyrosine was synthesized, and its transport kinetics were studied in freshly cultured rat hepatocytes. Uptake into hepatocytes was time and temperature dependent and was decreased by the inhibitors diisothiocyandisulfonic acid stilbene, probenecid and carbonyl cyanide chlorophenyl hydrazone, demonstrating carrier mediation and energy dependence. At concentrations of iodinated cholyl-glycyl-tyrosine less than 10 mumol/L, uptake was 27% +/- 5% sodium dependent, whereas at concentrations from 10 mumol/L to 40 mumol/L uptake was 52% +/- 4% sodium dependent. The apparent affinity for uptake of 125I-labeled cholyl-glycyl-tyrosine was 8 +/-

Searcher : Shears 571-272-2528

2  $\mu\text{mol/L}$ , and the maximal velocity was  $50 \pm 20$  pmol/micrograms DNA/min. Both taurocholate and indocyanine green inhibited uptake of  $^{125}\text{I}$ -labeled cholyl-glycyl-tyrosine. Indocyanine green inhibited the uptake of  $^{125}\text{I}$ -labeled cholyl-glycyl-tyrosine ( $K_i = 10$  microns) more effectively than taurocholate ( $K_i = 20$  microns). We conclude that  $^{125}\text{I}$ -labeled cholyl-glycyl-tyrosine is not a specific probe for either sodium-dependent bile salt or sodium-independent organic anion carriers, but appears to use both systems in a concentration-dependent manner in cultured rat hepatocytes.

L27 ANSWER 2 OF 7 MEDLINE on STN  
 ACCESSION NUMBER: 89341629 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 2760550  
 TITLE: Characterization of sarcosylsarcosodeoxycholic acid formed during the synthesis of sarcosodeoxycholic acid.  
 AUTHOR: Batta A K; Salen G; Shefer S  
 CORPORATE SOURCE: Department of Medicine, UMDN-NJ Medical School, Newark 07103.  
 CONTRACT NUMBER: AM-18707 (NIADDK)  
 AM-26756 (NIADDK)  
 HL-17818 (NHLBI)  
 SOURCE: Journal of lipid research, (1989 May) 30 (5) 771-4.  
 Journal code: 0376606. ISSN: 0022-2275.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198909  
 ENTRY DATE: Entered STN: 19900309  
 Last Updated on STN: 19970203  
 Entered Medline: 19890915

AB This report describes the isolation of sarcosylsarcosine conjugate of ursodeoxycholic acid (UDCA) formed during the synthesis of sarcoUDCA by the mixed anhydride method. The compound was characterized by its chemical ionization mass spectrum. The diamino acid conjugate was formed only when the free amino acid was used for conjugation. This was confirmed by the isolation of glycylglycoUDCA during the conjugation of UDCA with free glycine but not with glycine ethyl ester hydrochloride. Pure sarcoUDCA was prepared by conjugation of UDCA with sarcosine methyl ester hydrochloride while sarcoUDCA on further reaction with the protected sarcosine derivative gave pure sarcosylsarcoUDCA in 52% yield.

L27 ANSWER 3 OF 7 MEDLINE on STN  
 ACCESSION NUMBER: 89194027 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 2784686  
 TITLE: Effect of anaesthetic agents on bile flow and biliary excretion of  $^{131}\text{I}$ -cholylglycyltyrosine in the rat.  
 AUTHOR: Mills C O; Freeman J F; Salt P J; Elias E  
 CORPORATE SOURCE: Department of Medicine, Queen Elizabeth Hospital, Birmingham.  
 SOURCE: British journal of anaesthesia, (1989 Mar) 62 (3) 311-5.  
 Journal code: 0372541. ISSN: 0007-0912.  
 PUB. COUNTRY: ENGLAND: United Kingdom

10/088807

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198905  
ENTRY DATE: Entered STN: 19900306  
Last Updated on STN: 19970203  
Entered Medline: 19890524

AB We have compared in the rat the effects of i.v. anaesthetic agents on bile flow rate and on the biliary excretion of a novel bile acid, 131I-cholyglycyltyrosine (131I-cholygly.tyr.). Etomidate 1-mg bolus and 2-mg h-1 infusion, Althesin 3-mg bolus and 14.5-mg h-1 infusion and propofol 3.3-mg bolus and 3.3-mg h-1 were given via a tail vein cannula and pentobarbitone 50 mg kg-1 was given by the intraperitoneal route, to groups of six rats. Each animal received only one anaesthetic agent. One hour after cannulation of the common bile duct, 131I-cholygly.tyr. 5 microCi was injected into the jugular vein and bile was collected every 1 min for 10 min. The mean (SD) percentage cumulative biliary excretion of 131I-cholygly.tyr. at the end of 10 min was: propofol group 74.1 (5.2)%; Althesin group 82.3 (2.2)%; etomidate group 69.4 (17.6)%; pentobarbitone group 76.4 (3.2)%. Propofol and Althesin were relatively more choleric, causing bile flow rates twice that produced by pentobarbitone. Only Althesin caused a significant increase in biliary excretion of 131I-cholygly.tyr. relative to that in rats that received pentobarbitone. Bile flow rates for the respective anaesthetic techniques (microliter min-1/100 g body weight) (mean (SD)) were: propofol group 14.1 (1.8); Althesin group 12.5 (1.7); etomidate 8.5 (1.4); pentobarbitone group 7.3 (1.0). There was a marked metabolic acidosis in all rats except in the propofol group, in which normal acid-base status and oxygenation were observed.

L27 ANSWER 4 OF 7 MEDLINE on STN  
ACCESSION NUMBER: 87203176 MEDLINE  
DOCUMENT NUMBER: PubMed ID: 3574993  
TITLE: Absence of an acinar gradient for bile acid uptake in developing rat liver.  
AUTHOR: Suchy F J; Balistreri W F; Breslin J S; Dumaswala R; Setchell K D; Garfield S A  
CONTRACT NUMBER: HD-20632 (NICHD)  
HL-0727-5,2-05800-1391 (NHLBI)  
SOURCE: Pediatric research, (1987 Apr) 21 (4) 417-21.  
Journal code: 0100714. ISSN: 0031-3998.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198706  
ENTRY DATE: Entered STN: 19900303  
Last Updated on STN: 19970203  
Entered Medline: 19870610

AB We studied the acinar distribution for uptake of the bile acid analogue [125I]-cholyglycyltyrosine in livers from adult and 14-day-old suckling rats. Portal and peripheral (systemic) serum bile acid concentrations were also measured by combined gas chromatography-mass spectrometry as an independent index of hepatic

bile acid clearance from portal blood. Utilizing light microscopic autoradiography, a steep, decreasing portal to centrilobular gradient for cholyglycyltyrosine uptake was noted in adult rat liver. In contrast, there was no lobular gradient for cholyglycyltyrosine uptake visible in the 14-day-rat liver; all hepatocytes within the acinus contained a similar number of silver grains. Portal vein total bile acid concentrations were significantly higher in serum of adult compared to 14-day-old rats. In contrast, bile acid concentrations were 10-fold higher in the peripheral serum of developing versus adult rats. The peripheral to portal serum bile acid concentration ratio was 0.23 in the adult and 6.48 in the 14-day-old rat. We conclude that the entire hepatic lobule participates in the uptake of bile acids in the 14-day-old rat even under the basal conditions of this study. The normal "reserve" function of centrilobular hepatocytes is not sufficient to compensate for the decreased transport capacity of the developing liver with the result that increased concentrations of bile acids enter and accumulate in the systemic circulation.

L27 ANSWER 5 OF 7 MEDLINE on STN  
 ACCESSION NUMBER: 86192567 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 3699064  
 TITLE: Iodinated cholyglycyltyrosine: a new agent for hepatobiliary imaging.  
 AUTHOR: Clements D; Mills C; Iqbal S; Chandler S; Elias E  
 SOURCE: European journal of nuclear medicine, (1986) 11 (10) 401-4.  
 Journal code: 7606882. ISSN: 0340-6997.  
 PUB. COUNTRY: GERMANY, WEST: Germany, Federal Republic of  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 198605  
 ENTRY DATE: Entered STN: 19900321  
 Last Updated on STN: 19970203  
 Entered Medline: 19860527

AB The characteristics of radiolabelled cholyglycyltyrosine (CGT), a recently synthesised bile acid, were studied.  $^{125}\text{I}$ -CGT-Na was found to have a short plasma half-life of  $1.6 \pm 0.4$  min in rats and  $3.1 \pm 0.7$  min in dogs. Biliary clearance studies showed the cumulative biliary output of the tracer over 20 min in rats to be 95.7% of the total dose administered, with a mean biliary transit time (50% retention time) of  $4.0 \pm 0.1$  min, i.e. similar to the biliary kinetics of taurocholate.  $^{131}\text{I}$ -CGT-Na proved to be satisfactory for hepatobiliary imaging in rats and dogs at doses of 35 microCi (1.3 MBq) in rats and 90 microCi (3.3 MBq) in dogs. Satisfactory hepatic images were also obtained in rats that had high bilirubin levels produced by obstruction or the recycling of bile. These results show that CGT has better pharmacokinetics than currently used hepatobiliary imaging agents, and that this new compound may be useful in scintigraphy even in the presence of jaundice.

L27 ANSWER 6 OF 7 MEDLINE on STN  
 ACCESSION NUMBER: 86060721 MEDLINE  
 DOCUMENT NUMBER: PubMed ID: 4067252

TITLE: Selectively reduced biliary excretion of cholyldiglycylhistamine but not of cholyltetraglycylhistamine in ethinyl estradiol-treated rats. A possible indicator of increased bile canalicular permeability.

AUTHOR: Mills C O; Iqbal S; Elias E

SOURCE: Journal of hepatology, (1985) 1 (3) 199-210.  
Journal code: 8503886. ISSN: 0168-8278.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 198601

ENTRY DATE: Entered STN: 19900321  
Last Updated on STN: 19900321  
Entered Medline: 19860114

AB A series of bile acid derivatives were synthesized, purified and radiolabelled. These were [125I]cholylglycylhistamine [( 125I)CGH), [125I] cholyldiglycylhistamine [( 125I)CG2H), [125I]cholyltriglycylhistamine [( 125I)CG3H), and [125I]cholyltetraglycylhistamine [( 125I)CG4H). These derivatives were rapidly excreted unchanged into the bile of bile-fistula rats. In normal rats the 30-min cumulative excretion following intravenous administration was only 39.0 +/- 0.7% for [125I]CGH but greater than 80% for the three larger compounds. This marked difference in biliary recovery between CGH and the other larger compounds could be due to a threshold biliary permeability, and we postulated that the critical molecular weight threshold for effective biliary retention of such compounds falls between [125I]CGH (MW 683) and [125I]CG2H (MW 740). Increased permeability, involving a shift to a higher molecular weight threshold would then be anticipated to diminish biliary excretion of [125I]CG2H (MW 740) before exerting a major influence on the biliary excretion of [125I]CG4H (MW 854). We previously reported functional and morphological studies which suggest that ethinyl estradiol (EE) may alter the permeability of bile canalicular tight junctions. In this study we have looked for further evidence of a progressive permeability change in EE-induced cholestasis by observing the biliary excretion of CG2H and CG4H in rats. Treatment with EE (5 mg/kg/day) for 3 days (EE3) or with the injection vehicle propylene glycol for 7 days (C7) reduced biliary excretion to a significant extent when compared to 3-day controls (C3) but had no differential effect on the 30-min recoveries from bile of CG2H and CG4H, respectively: C3 (81.2 +/- 1.8% and 81.7 +/- 2.1%, P = CN): C7 (72.3 +/- 3.0% and 73.5 +/- 3.6%, P = NS): EE3 61.8 +/- 2.5% and 61.9 +/- 2.7%, P = NS). However, treatment with EE for 7 days significantly reduced the biliary recovery of CG2H (46.8 +/- 9%) compared to EE3 rats (P less than 0.0025) but there was no significant change of biliary CG4H recovery (61.0 +/- 2.5%, P = NS) compared with EE3 rats. These results are compatible with our hypothesis that EE-induced cholestasis is associated with a change of biliary permeability which, as it progresses, affects successively larger molecules.

L27 ANSWER 7 OF 7 MEDLINE on STN

ACCESSION NUMBER: 84049770 MEDLINE

DOCUMENT NUMBER: PubMed ID: 6638192

10/088807

TITLE: Intracellular bile acid transport in rat liver as visualized by electron microscope autoradiography using a bile acid analogue.  
AUTHOR: Suchy F J; Balistreri W F; Hung J; Miller P; Garfield S A  
CONTRACT NUMBER: AM-27097 (NIADDK)  
HD-16907 (NICHD)  
SOURCE: American journal of physiology, (1983 Nov) 245 (5 Pt 1) G681-9.  
Journal code: 0370511. ISSN: 0002-9513.  
PUB. COUNTRY: United States  
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
LANGUAGE: English  
FILE SEGMENT: Priority Journals  
ENTRY MONTH: 198312  
ENTRY DATE: Entered STN: 19900319  
Last Updated on STN: 19970203  
Entered Medline: 19831217

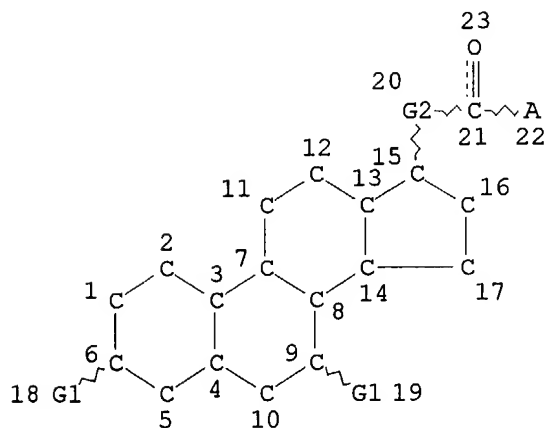
AB The role of hepatocyte organelles in the intracellular transport and secretion of conjugated bile acids has not been defined. Therefore we studied the transport and observed the subcellular localization of the bile acid analogue 125I-cholylglycyltyrosine by electron microscope autoradiography to further understand the possible compartmentation of bile acids within the hepatocyte. 125I-cholylglycyltyrosine, which retains a net negative charge, exhibited transport properties similar to native bile acids. After portal vein injection, the compound was recovered intact from bile, and the pattern of excretion paralleled that of [14C]cholylglycine. In addition, cholylglycyltyrosine uptake by isolated hepatocytes was sodium dependent. For autoradiography the analogue was injected into the portal vein, and the liver was perfusion fixed after 30 or 300 s. Light microscope autoradiography performed 30 s after isotope injection demonstrated a steep periportal-to-centrilobular gradient for 125I-cholylglycyltyrosine uptake. At 30 s quantitative grain analysis of electron microscope autoradiographs showed predominant labeling of the plasma membrane and the smooth endoplasmic reticulum (SER). The grain distribution over the region of the plasma membrane decreased from 15% at 30 s to 7% by 300 s and was associated with a sevenfold increase in labeling of the Golgi apparatus and a sixfold increase in labeling of the pericanalicular region. Grain distribution over the SER at 300 s was the same as that noted at 30 s. The hypothesis is presented that bile acids move from the sinusoidal plasma membrane to bile via a pathway that includes the SER and Golgi apparatus.

FILE 'HOME' ENTERED AT 12:28:09 ON 28 JUL 2004

10/088807

(FILE 'REGISTRY' ENTERED AT 11:59:06 ON 28 JUL 2004)

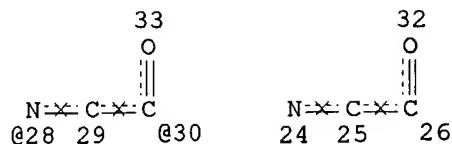
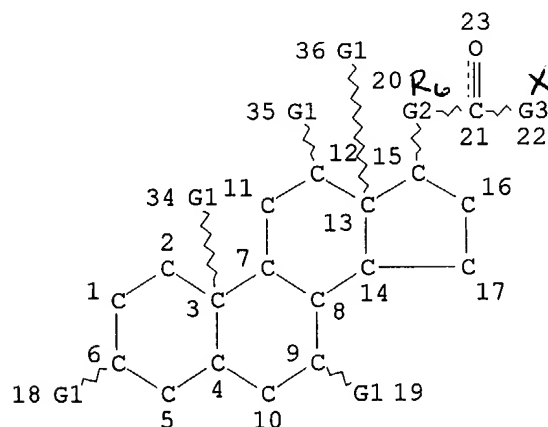
L1 STR



VAR G1=OH/H/ET/ME/I-PR/N-PR/I-BU/N-BU/S-BU/T-BU  
REP G2=(2-6) C  
NODE ATTRIBUTES:  
NSPEC IS RC AT 22  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:  
RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 23

STEREO ATTRIBUTES: NONE  
L2 14357 SEA FILE=REGISTRY SSS FUL L1  
L17 STR



\* Allows for  $\geq 2$  peptides

VAR G1=OH/H/ET/ME/I-PR/N-PR/I-BU/N-BU/S-BU/T-BU  
REP G2=(2-6) C  
VAR G3=28/30  
NODE ATTRIBUTES:  
NSPEC IS RC AT 24  
NSPEC IS RC AT 26

10/088807

NSPEC IS RC AT 28  
NSPEC IS RC AT 30  
CONNECT IS X2 RC AT 1  
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DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC I

NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE

L18 322 SEA FILE=REGISTRY SUB=L2 SSS FUL L17  
L19 273 SEA FILE=REGISTRY ABB=ON PLU=ON L18 AND 1/NC

(FILE 'CAPLUS' ENTERED AT 12:00:58 ON 28 JUL 2004)

L20 91 S L19  
L21 49 S L20 NOT (PY=>1999 OR PD=>19990730)

L21 ANSWER 1 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 02 Feb 1999

ACCESSION NUMBER: 1999:68262 CAPLUS

DOCUMENT NUMBER: 130:278125

TITLE: Signal transmission by artificial receptors  
embedded in bilayer membranes

AUTHOR(S): Kikuchi, Jun-Ichi

CORPORATE SOURCE: Institute for Fundamental Research of Organic  
Chemistry, Kyushu University, Fukuoka, 812-81,  
Japan

SOURCE: Molecular Recognition and Inclusion, Proceedings  
of the International Symposium on Molecular  
Recognition and Inclusion, 9th, Lyon, Sept.  
7-12, 1996 (1998), Meeting Date 1996, 129-134.  
Editor(s): Coleman, Annette W. Kluwer:  
Dordrecht, Neth.  
CODEN: 67FSAY

DOCUMENT TYPE: Conference

LANGUAGE: English

AB The authors designed steroid cyclophanes as artificial cell-surface  
receptors. Each steroid cyclophane has three functional components:  
a 1,6,20,25-tetraaza[6.1.6.1]paracyclophane ring, four bile acid  
moieties and four L-lysine residues connecting them. They employ  
hydrophobic aromatic guests and metal ions as signaling ligands and  
signal transmitters, resp., for the steroid cyclophanes.

IT 182889-23-2 183072-82-4 220527-51-5  
220527-56-0

RL: BPR (Biological process); BSU (Biological study, unclassified);

BIOL (Biological study); PROC (Process)

(artificial receptor; signal transmission by artificial receptors  
embedded in bilayer membranes)

REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE

10/088807

FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 01 Feb 1999  
ACCESSION NUMBER: 1999:64222 CAPLUS  
DOCUMENT NUMBER: 130:332204  
TITLE: Design and assay of inhibitors of HIV-1 Vpr cell  
killing and growth arrest activity using  
microbial assay systems  
AUTHOR(S): Sankovich, Sonia E.; Koleski, Daniela; Baell,  
Jonathan; Matthews, Barry; Azad, Ahmed A.;  
Macreadie, Ian G.  
CORPORATE SOURCE: Biomolecular Research Institute, Parkville,  
3052, Australia  
SOURCE: Journal of Biomolecular Screening (1998), 3(4),  
299-304  
CODEN: JBISF3; ISSN: 1087-0571  
PUBLISHER: Mary Ann Liebert, Inc.  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB Viral protein R (Vpr), one of the accessory gene products encoded by  
the human immunodeficiency virus type 1 (HIV-1) genome, has a number of  
functions, including causing a growth arrest of HIV-1-infected cells  
and possibly the death of uninfected bystander cells. In microbial  
assay systems, the C-terminal portion of Vpr can cause cell death  
when added externally, and when expressed in yeast it causes growth  
arrest. In this study we have sought to obtain inhibitors of the  
Vpr functions that affect the microbial systems. Our first approach  
employed peptide display, which identified a number of sequences,  
including a heptapeptide sequence, GETRAPL, involved in binding to  
the C-terminus of Vpr. To determine whether GETRAPL could block the  
extracellular cytotoxic activity of Vpr, the heptapeptide was  
synthesized and found to have some blocking activity in microbial  
assays. A second approach led to the finding that melittin  
inhibitors had activity against Vpr extracellular activities. In a  
third approach, compds. were tested against the Vpr-induced growth  
arrest. A number of compds. were found to abrogate the growth arrest,  
and some also inhibited Vpr's extracellular activity.  
IT 205587-95-7 205588-02-9 205588-97-2  
RL: ANT (Analyte); BAC (Biological activity or effector, except  
adverse); BSU (Biological study, unclassified); THU (Therapeutic  
use); ANST (Analytical study); BIOL (Biological study); USES (Uses)  
(design and assay of inhibitors of HIV-1 Vpr cell killing and  
growth arrest activity using microbial assay systems)  
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 12 Jan 1999  
ACCESSION NUMBER: 1999:19116 CAPLUS  
DOCUMENT NUMBER: 130:179092  
TITLE: Steroid cyclophanes as artificial cell-surface  
receptors. Molecular recognition and its  
consequence in signal transduction behavior

Searcher : Shears 571-272-2528

10/088807

AUTHOR(S): Kikuchi, Jun-Ichi; Murakami, Yukito  
CORPORATE SOURCE: Institute for Fundamental Research in Organic  
Chemistry, Kyushu University, Fukuoka, 812-8581,  
Japan  
SOURCE: Journal of Inclusion Phenomena and Molecular  
Recognition in Chemistry (1998), 32(2-3),  
209-221  
CODEN: JIMCEN; ISSN: 0923-0750  
PUBLISHER: Kluwer Academic Publishers  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Steroid cyclophanes, bearing four bile acid moieties covalently  
placed on a tetraazaparacyclophane skeleton, were designed and  
synthesized as artificial cell-surface receptors. Guest-binding  
behavior of the steroid cyclophanes embedded in a bilayer membrane  
formed with a synthetic peptide lipid was clarified by means of  
fluorescence and CD spectroscopy. We found that the steroid  
cyclophane effectively bound aromatic guests in both bilayer membranes  
and aqueous solution. In addition, copper(II) ions acted as a guest species  
for the steroid cyclophane and a competitive inhibitor toward a  
NADH-dependent lactate dehydrogenase (LDH). On these grounds, we  
constituted a supramol. assembly as an artificial signaling system  
in combination with the steroid cyclophane, a cationic peptide  
lipid, and LDH. As a consequence, the steroid cyclophane acted as  
an effective artificial cell-surface receptor being capable of  
transmitting an external signal to the enzyme in collaboration with  
copper(II) ions as a signal transmitter.

IT 156881-79-7P 182889-23-2P 183072-82-4P  
220527-51-5P 220527-56-0P

RL: BPR (Biological process); BSU (Biological study, unclassified);  
PRP (Properties); SPN (Synthetic preparation); BIOL (Biological  
study); PREP (Preparation); PROC (Process)

(preparation and characterization of steroid cyclophanes as artificial  
cell-surface receptors)

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 Jan 1999

ACCESSION NUMBER: 1999:17661 CAPLUS

DOCUMENT NUMBER: 130:257244

TITLE: Low-density lipoprotein receptor-mediated  
delivery of a lipophilic daunorubicin derivative  
to B16 tumors in mice using apolipoprotein  
E-enriched liposomes

AUTHOR(S): Versluis, A. J.; Rensen, P. C. N.; Rump, E. T.;  
Van Berkel, T. J. C.; Bijsterbosch, M. K.

CORPORATE SOURCE: Division of Biopharmaceutics, Leiden/Amsterdam  
Center for Drug Research, University of Leiden,  
Leiden, 2300 RA, Neth.

SOURCE: British Journal of Cancer (1998), 78(12),  
1607-1614

CODEN: BJCAAI; ISSN: 0007-0920

PUBLISHER: Churchill Livingstone

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Many tumors express relatively high levels of low-d. lipoprotein (LDL) receptors on their membranes. The LDL receptor is, therefore, an attractive target for the selective delivery of antineoplastic drugs to tumor cells. We reported previously on the synthesis of small apolipoprotein E (apoE)-containing liposomes that behave in vivo in a very similar way to native LDL. In this study, we examined the interaction of this liposomal carrier with cultured B16 melanoma cells. Binding of apoE liposomes to the cells is saturable, with a maximum binding of approx. 90 000 particles per cell. Cross-competition studies indicated that apoE liposomes are bound by the LDL receptor. Association of apoE liposomes to B16 cells is strictly  $\text{Ca}^{2+}$  dependent, which forms addnl. evidence for a role of the LDL receptor. The affinity of apoE liposomes for the LDL receptor on B16 cells is 15-fold higher than that of LDL (0.77 vs 11.5 nM resp.). ApoE is essential for the LDL receptor recognition because liposomes lacking apoE were, in competition studies, 20- to 50-fold less effective than apoE-containing liposomes. We examined in B16 tumor-bearing mice the tumor-localizing properties of apoE liposomes and the disposition of an incorporated lipophilic derivative of daunorubicin (LAD). Tissue distribution studies showed that LAD-loaded apoE liposomes were taken up and processed by the major LDL receptor-expressing organs (i.e. adrenals, liver and spleen). Of all other tissues, the tumor showed the highest uptake. The distribution patterns of LAD-loaded apoE liposomes and native LDL in the tumor-bearing mice were very similar, which supports the role of the LDL receptor in the disposition of the prodrug-loaded particles. The disposition of LAD followed the pattern of the liposomal carrier. We conclude that apoE liposomes enable LDL receptor-mediated specific delivery of antineoplastic (pro)drugs to tumors, and, therefore, constitute an attractive novel option for antitumor chemotherapy.

IT 208237-67-6

RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(LDL receptor-mediated delivery of lipophilic daunorubicin derivative to B16 tumors in mice using apolipoprotein E-enriched liposomes)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L21 ANSWER 5 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 30 May 1998

ACCESSION NUMBER: 1998:322821 CAPLUS

DOCUMENT NUMBER: 129:45208

TITLE: Synthesis of a lipophilic daunorubicin derivative and its incorporation into lipidic carriers developed for LDL receptor-mediated tumor therapy

AUTHOR(S): Versluis, A. Jenny; Rump, Erik T.; Rensen, Patrick C. N.; Van Berkel, Theo J. C.; Bijsterbosch, Martin K.

CORPORATE SOURCE: Division of Biopharmaceutics, Leiden/Amsterdam Center for Drug Research, Univ. of Leiden, Leiden, 2300 RA, Neth.

SOURCE: Pharmaceutical Research (1998), 15(4), 531-537  
CODEN: PHREEB; ISSN: 0724-8741  
PUBLISHER: Plenum Publishing Corp.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Many tumors express elevated levels of LDL receptors (apoB, E receptors) on their membranes. Selective delivery of antineoplastic drugs to tumors by incorporation of these drugs into LDL or LDL-resembling particles should improve the efficacy of tumor therapy and minimize the severe side-effects. Since the apolipoproteins on the particles are essential for the LDL receptor recognition, drugs should preferably be incorporated into the lipid moiety. Most antitumor agents are too hydrophilic for incorporation into these carriers. Methods. We synthesized LAD, a lipophilic prodrug of daunorubicin, by coupling the drug via a lysosomally degradable peptide spacer to a cholesteryl oleate analog. The overall yield of the synthesis was 50% with a purity of >90%. Radioactivity ([<sup>3</sup>H]) labeled LAD was obtained via a slightly modified procedure (yield 40%). The octanol/water partition coefficient of LAD is 30-fold higher than that of daunorubicin. LAD could be incorporated into triglyceride-rich lipid emulsions and small liposomes, which, if provided with apoE, have been demonstrated earlier to be cleared in vivo via the LDL receptor. The liposomes contained approx. 10 mols. of LAD per liposomal particle. Anal. of differently sized LAD-containing emulsions suggests that LAD assoc. with the surfaces of lipidic particles. In the presence of human serum, LAD did not dissociate from the emulsion particles, indicating a firm association of LAD with the carrier. The coupling of a cholesterol ester analog to daunorubicin results in a lipophilic prodrug that can be firmly anchored into lipidic carriers. LAD-loaded emulsions and liposomes provided with recombinant apoE will be tested in the near future for their ability to deliver LAD to tumor tissue in vivo via the LDL receptor.

IT 208294-95-5P

RL: BPR (Biological process); BSU (Biological study, unclassified);  
SPN (Synthetic preparation); BIOL (Biological study); PREP  
(Preparation); PROC (Process)

(preparation of a lipophilic daunorubicin derivative and its  
incorporation  
into lipid carriers developed for LDL receptor-mediated tumor  
therapy)

IT 208237-67-6P

RL: BPR (Biological process); BSU (Biological study, unclassified);  
SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological  
study); PREP (Preparation); PROC (Process); USES (Uses)

(preparation of a lipophilic daunorubicin derivative and its  
incorporation  
into lipid carriers developed for LDL receptor-mediated tumor  
therapy)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 6 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 04 Mar 1998

ACCESSION NUMBER: 1998:127741 CAPLUS

10/088807

DOCUMENT NUMBER: 128:254869  
TITLE: Molecular modeling of the intestinal bile acid carrier: a comparative molecular field analysis study  
AUTHOR(S): Swaan, Peter W.; Szoka, Francis C., Jr.; Oie, Svein  
CORPORATE SOURCE: Department of Biopharmaceutical Sciences, University of California, San Francisco, CA, 94143-0446, USA  
SOURCE: Journal of Computer-Aided Molecular Design (1997), 11(6), 581-588  
CODEN: JCADEQ; ISSN: 0920-654X  
PUBLISHER: Kluwer Academic Publishers  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A structure-binding activity relationship for the intestinal bile acid transporter has been developed using data from a series of bile acid analogs in a comparative mol. field anal. (CoMFA). The studied compds. consisted of a series of bile acid-peptide conjugates, with modifications at the 24 position of the cholic acid sterol nucleus, and compds. with slight modifications at the 3, 7, and 12 positions. For the CoMFA study, these compds. were divided into a training set and a test set, comprising 25 and 5 mols., resp. The best three-dimensional quant. structure-activity relationship model found rationalizes the steric and electrostatic factors which modulate affinity to the bile acid carrier with a cross-validated, conventional and predictive  $r^2$  of 0.63, 0.96, and 0.69, resp., indicating a good predictive model for carrier affinity. Binding is facilitated by positioning an electroneg. moiety at the 24-27 position, and also by steric bulk at the end of the side chain. The model suggests substitutions at positions 3, 7, 12, and 24 that could lead to new substrates with reasonable affinity for the carrier.

IT 205238-74-0 205238-76-2 205238-77-3  
205238-78-4 205238-79-5 205238-80-8  
205238-81-9 205238-82-0 205238-83-1  
205238-84-2 205239-05-0

RL: BPR (Biological process); BSU (Biological study, unclassified);  
BIOL (Biological study); PROC (Process)  
(mol. modeling of intestinal bile acid carrier)

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE  
FOR THIS RECORD. ALL CITATIONS AVAILABLE  
IN THE RE FORMAT

L21 ANSWER 7 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 14 Feb 1998

ACCESSION NUMBER: 1998:87618 CAPLUS

DOCUMENT NUMBER: 128:154278

TITLE: synthesis and biological activity of polysulfolithocolic acid amides as growth factor receptor inhibitors

INVENTOR(S): Kogan, Timothy P.; Biediger, Ronald J.; Stephan, Clifford C.; Tilton, Ronald G.; Scott, Ian L.; Brock, Tommy A.

PATENT ASSIGNEE(S): Texas Biotechnology Corp., USA

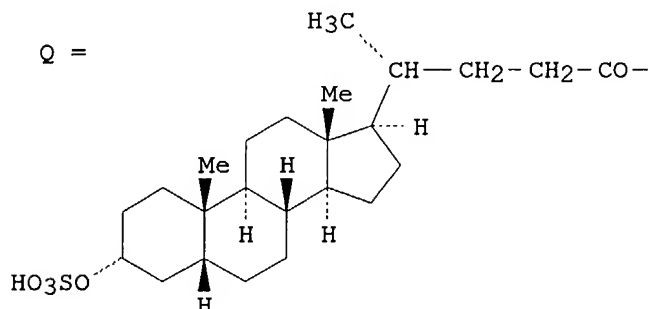
SOURCE: PCT Int. Appl., 41 pp.

Searcher : Shears 571-272-2528

10/088807

DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9803181	A1	19980129	WO 1997-US13103	19970722
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9740462	A1	19980210	AU 1997-40462	19970722
PRIORITY APPLN. INFO.:			US 1996-22039P	P 19960722
			WO 1997-US13103	W 19970722
OTHER SOURCE(S):		MARPAT 128:154278		
GI				



AB Synthesis of polysulfolithocolic acid amides [QLys(Q)]2X (I) or Q2X where X is any diamine are described. This invention is also directed to pharmaceutical compns. (no data) and methods of inhibiting cellular proliferation using these compds. Thus, I [X = NH(CH2)5NH] (II) was prepared in four steps by the amidation of lithocholic acid with lysine Me ester, deesterification, amidation with 1,5-pentanediamine and sulfonylation with sulfur trioxide and pyridine. II at a 30uM concentration showed a 72% inhibition of serum-stimulated HASMC proliferation.

IT **202590-23-6P 202590-25-8P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(synthesis and biol. activity of polysulfolithocolic acid amides as growth factor receptor inhibitors)

IT **202590-22-5P 202590-24-7P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);

10/088807

RACT (Reactant or reagent)

(synthesis and biol. activity of polysulfolithocolic acid amides  
as growth factor receptor inhibitors)

IT 202590-26-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and biol. activity of polysulfolithocolic acid amides  
as growth factor receptor inhibitors)

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR  
THIS RECORD. ALL CITATIONS AVAILABLE IN  
THE RE FORMAT

L21 ANSWER 8 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 06 Aug 1997

ACCESSION NUMBER: 1997:492799 CAPLUS

DOCUMENT NUMBER: 127:121912

TITLE: Preparation of bile acid inhibitors of matrix  
metalloproteinase enzymes

INVENTOR(S): Jacobson, Alan R.; Gabler, Douglas G.;  
Oleksyszyn, Jozef

PATENT ASSIGNEE(S): Osteoarthritis Sciences, Inc., USA

SOURCE: U.S., 10 pp., Cont. of U. S. Ser. No. 224,427,  
abandoned.

CODEN: USXXAM

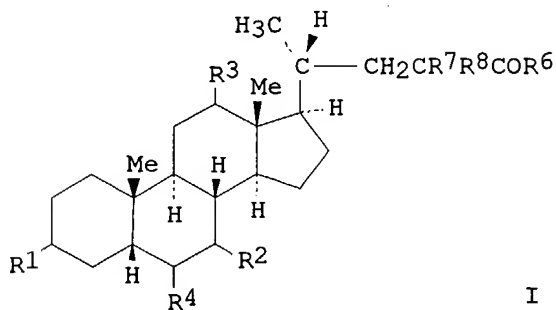
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 5646316	A	19970708	US 1995-430129	19950425
PRIORITY APPLN. INFO.:			US 1994-224427	19940408
OTHER SOURCE(S):	MARPAT 127:121912			
GI				



AB Bile acid derivs. I [R1, R2, R3, R4 = H, OH, OR5, S(O)R5, SO2R5, SO3R5, NR5; R5 = (un)substituted alkyl, aryl, heteroaryl; R6 = (NR11CR9R10CO)nNHOH; R7, R8, R9, R11 = (un)substituted alkyl, aryl, heteroaryl; R10 = (un)substituted alkyl, aryl, heteroaryl, side chain of an amino acid; aryl = Ph, naphthyl, anthracyl; heteroaryl = pyridyl, benzothienyl, indolyl, quinolinyl,

Searcher : Shears 571-272-2528

phenothiazinyl; n = 1, 2] were prepared I was prepared via reaction of lithocholic acid with L-leucine hydroxamate in DMF containing hydroxybenzotriazole followed by treatment of the mixture with dicyclohexylcarbodiimide. I is an active inhibitor of metalloproteinase enzymes (IC<sub>50</sub> = 1 μM vs. stromelysin; 27% inhibition at 10 μM vs. collagenase; IC<sub>50</sub> = 300 nM vs. gelatinase).

IT 192876-15-6P 192876-16-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of bile acid inhibitors of matrix metalloproteinase enzymes)

L21 ANSWER 9 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 Jul 1997

ACCESSION NUMBER: 1997:433596 CAPLUS

DOCUMENT NUMBER: 127:70711

TITLE: Enhanced Transepithelial Transport of Peptides by Conjugation to Cholic Acid

AUTHOR(S): Swaan, Peter W.; Hillgren, Kathleen M.; Szoka, Francis C. Jr.; Oie, Svein

CORPORATE SOURCE: Department of Biopharmaceutical Sciences, University of California at San Francisco, San Francisco, CA, 94143-0446, USA

SOURCE: Bioconjugate Chemistry (1997), 8(4), 520-525  
CODEN: BCCHES; ISSN: 1043-1802

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The potential of the intestinal bile acid transporter to serve as a shuttle for small peptide mols. was investigated. Eleven peptides with a 2-6 amino acid backbone were conjugated to the 24-position of 3α,7α,12α-trihydroxy-5β-cholan-24-oic acid (cholic acid) via an amide bond using an automated peptide synthesizer. In a human intestinal cell line (CaCo-2), cholic acid-peptide conjugates were able to inhibit the transepithelial transport of [3H]taurocholic acid, a natural substrate for the bile acid carrier, at a 100:1 conjugate/substrate ratio. Affinity for the carrier decreased significantly when the conjugate in the 24-position increased from 1 to 2 amino acids. Further increase in the amino acid chain length caused only minor decrease in affinity. A tetrapeptide-bile acid conjugate, [3H]ChEAAA (Ch = cholic acid), was transported by the bile acid transporter, showing markedly higher apical (AP)-to-basolateral (BL) compared to BL-to-AP transport and inhibition by a 100-fold excess taurocholic acid. Another conjugate with 6 amino acids (ChEASASA) was transported by a passive diffusion pathway but still showed higher transport rates than the passive permeability marker mannitol, suggesting the possibility that the cholic acid moiety aids the passive membrane transfer of peptide mols. by increasing its lipophilicity. Metabolism of bile acid-peptide conjugates in CaCo-2 cells was 3% over 3 h. In conclusion, these studies show that the coupling of peptides to the 24-position of the sterol nucleus in cholic acid results in a combination of decreased metabolism and increased intestinal absorption,

either by a carrier-mediated pathway or by accelerated passive diffusion.

IT 191528-84-4 191528-85-5 191528-86-6  
191528-87-7 191528-88-8 191528-89-9  
191528-90-2 191528-91-3 191528-92-4  
191528-93-5 191528-94-6

RL: BPR (Biological process); BSU (Biological study, unclassified);  
BIOL (Biological study); PROC (Process)  
(enhanced transepithelial transport of peptides by conjugation to  
cholic acid)

L21 ANSWER 10 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 04 Apr 1997

ACCESSION NUMBER: 1997:218959 CAPLUS

DOCUMENT NUMBER: 126:308684

TITLE: Use of the intestinal bile acid transporter for  
the uptake of cholic acid conjugates with HIV-1  
protease inhibitory activity

AUTHOR(S): Kagedahle, Matts; Swaan, Peter W.; Redemann,  
Carl T.; Tang, Mary; Craik, Charles S.; Szoka,  
Francis C., Jr.; Oie, Svein

CORPORATE SOURCE: Dep. Pharmacy Pharmaceutical Chem., Univ.  
California, San Francisco, CA, 94143-0446, USA

SOURCE: Pharmaceutical Research (1997), 14(2), 176-180  
CODEN: PHREEB; ISSN: 0724-8741

PUBLISHER: Plenum

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The purpose of this study was to investigate the ability of the  
human intestinal bile acid transporter to transport cholic acid  
conjugates with potential HIV-1 protease inhibitory activity.  
Cholic acid was conjugated at the 24 position of the sterol nucleus  
with various amino acids and amino acid analogs. The CaCo-2 cell  
line was used as a model to investigate the interaction of these  
bile acid conjugates with the human intestinal bile acid  
transporter. Interaction between the carrier and the conjugates was  
quantified by inhibition of taurocholic acid transport and confirmed  
by transport of radiolabeled conjugates in this cell line. The  
highest interaction with the transporter, as quantified by  
inhibition of taurocholic acid transport, occurred when a single  
neg. charge was present around the 24 to 29 region of the sterol  
nucleus. A second neg. charge or a pos. charge significantly  
reduced the interaction. Transport of radiolabeled  
cholyl-L-Lys- $\epsilon$ -tBOC ester and cholyl-D-Asp- $\beta$ -benzyl  
ester was inhibited by taurocholic acid. Of all tested compds.,  
only cholyl-D-Asp- $\beta$ -benzyl ester showed modest HIV-1 protease  
inhibitory activity with an IC<sub>50</sub> of 125  $\mu$ M. Cholic acid-amino  
acid conjugates with appropriate stereochem. are recognized and  
transported by the human bile acid transporter and show modest HIV-1  
protease inhibitory activity. Transport of these conjugates by the  
bile acid carrier is influenced by charge and hydrophobicity around  
the 24 position of the sterol nucleus.

IT 189261-12-9P

RL: BAC (Biological activity or effector, except adverse); BPR  
(Biological process); BSU (Biological study, unclassified); PNU  
(Preparation, unclassified); THU (Therapeutic use); BIOL (Biological

10/088807

study); PREP (Preparation); PROC (Process); USES (Uses)  
(use of intestinal bile acid transporter for uptake of cholic  
acid conjugates with HIV-1 protease inhibitory activity)

L21 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 14 Mar 1997

ACCESSION NUMBER: 1997:173536 CAPLUS

DOCUMENT NUMBER: 126:246641

TITLE: Synthesis of steroidal analogs of gastrin and  
preliminary study on their bioactivities

AUTHOR(S): Weng, Lingling; Zhang, Xiao; Zheng, Hu

CORPORATE SOURCE: West China University of Medical Sciences,  
Changdu, 610041, Peop. Rep. China

SOURCE: Yaoxue Xuebao (1996), 31(9), 676-679

CODEN: YHHPAL; ISSN: 0513-4870

PUBLISHER: Chinese Academy of Medical Sciences, Institute  
of Materia Media

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

AB Steroid and oligopeptide compds. that are active on the  
gastrointestinal organs, were conjugated by using active ester  
method. 6 Steroid-oligopeptides were synthesized, and their  
structures were confirmed by spectral and elementary analyses.  
Preliminary study on their bioactivities showed that all these  
compds. were active and their duration of action were longer than  
the control sample.

IT 171511-54-9P 171511-55-0P 171511-58-3P  
171511-59-4P

RL: BAC (Biological activity or effector, except adverse); BSU  
(Biological study, unclassified); SPN (Synthetic preparation); BIOL  
(Biological study); PREP (Preparation)

(synthesis of steroidal analogs of gastrin and preliminary study  
on their bioactivities)

L21 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 17 Sep 1996

ACCESSION NUMBER: 1996:554339 CAPLUS

DOCUMENT NUMBER: 125:301305

TITLE: Circular dichroism of an aromatic guest induced  
by a chiral steroid cyclophane in aqueous  
solution and synthetic bilayer membrane

AUTHOR(S): Kikuchi, Jun-Ichi; Ogata, Toshiyuki; Inada,  
Masahiko; Murakami, Yukito

CORPORATE SOURCE: Inst. for Fundamental Res. in Organic Chem.,  
Kyushu Univ., Fukuoka, 812-81, Japan

SOURCE: Chemistry Letters (1996), (9), 771-772

CODEN: CMLTAG; ISSN: 0366-7022

PUBLISHER: Nippon Kagakkai

DOCUMENT TYPE: Journal

LANGUAGE: English

AB A steroid cyclophane, having L-lysine residues interposed between a  
tetraaza[6.1.6.1]paracyclophane skeleton and four cholate moieties,  
furnished a chiral binding site for a hydrophobic aromatic guest in a  
synthetic bilayer membrane as well as in aqueous solution, as evidence by  
induced CD.

IT 182889-23-2 183072-82-4

RL: BUU (Biological use, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process); USES (Uses)

(CD of an aromatic guest induced by a chiral steroid cyclophane in aqueous solution and synthetic bilayer membrane)

L21 ANSWER 13 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 18 Apr 1996

ACCESSION NUMBER: 1996:227067 CAPLUS

DOCUMENT NUMBER: 124:286366

TITLE: The fluorescence and CD study on the interaction of synthetic lipophilic hepatitis B virus preS(120-145) peptide analogs with phospholipid vesicles

AUTHOR(S): Cajal, Yoland; Rabanal, Francesc; Alsina, M. Asuncion; Reig, Francesca

CORPORATE SOURCE: Peptide Dep., CID-CSIC, Barcelona, 08034, Spain

SOURCE: Biopolymers (1996), 38(5), 607-18

CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: Wiley

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The interaction of the immunogenic peptide of human hepatitis B virus (HBV) preS(120-145), including B and T epitopes, with phospholipid vesicles has been studied by fluorescence techniques and CD. In addition, interaction of three lipopeptides derived from preS(120-145) containing stearyl, cholanoyl, and tripalmitoyl-S-glyceryl-cysteine (Pam3C) SS moieties with dipalmitoylphosphatidylcholine (DPPC) has been investigated by polarization fluorescence spectroscopy. Fluorescence expts. showed an increase in fluorescence intensity and a blue shift of the maximum emission wavelength upon interaction of preS(120-145) with DPPC vesicles below the transition temperature ( $T_c$ ), indicating that the tryptophan moiety enters a more hydrophobic environment. Moreover, fluorescence polarization expts. showed that the peptide decreased the membrane fluidity at the hydrophobic core, increasing the  $T_c$  of the lipid and decreasing the amplitude of the change of fluorescence polarization associated with the cooperative melting of 1,6-diphenyl-1,3,5-hexatriene labeled vesicles. The absence of leakage of vesicle-entrapped carboxyfluorescein indicates that the peptide did not promote vesicles lysis. Besides, the three lipopeptides derived from preS(120-145) showed a more pronounced rigidifying effect at the hydrophobic core of the bilayer, with a significant increase in the  $T_c$ . Stearyl- and cholanoyl-preS(120-145) restricted the motion of lipids also at the polar surface, whereas Pam3CSS-preS(120-145) did not alter the polar head group order. Finally, CD studies in 2,2,2-trifluoroethanol or in presence of vesicles suggested that the bound peptide adopted amphiphilic  $\alpha$ -helical and  $\beta$ -sheet structures, with an important contribution of the  $\beta$ -turn. It is concluded that preS(120-145) can interact with the lipid membrane through the formation of an amphipathic structure combination of  $\beta$ -sheet and  $\alpha$ -helix aligned parallel to the membrane surface, involving the N-terminal residues, and penetrating only a short distance into the hydrophobic core. The C-terminal part, with a combination of  $\beta$ -turn and  $\beta$ -sheet structure, remains at

10/088807

the outer part of the bilayer, being potentially accessible to immunocompetent cells. Furthermore, coupling of an hydrophobic moiety to the N-terminal part of the peptide favors anchoring to the membrane, probably facilitating interaction of the peptide with the Ig receptor. These results are in agreement with the induction of immune response by preS(120-145) and with the enhanced immunogenicity found in general for lipid-conjugated immunopeptides.

IT **134505-87-6**

RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)

(secondary structure of hepatitis B virus preS peptide and lipopeptide analogs in relation to membrane interaction and immunogenicity)

L21 ANSWER 14 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 13 Oct 1995

ACCESSION NUMBER: 1995:854259 CAPLUS

DOCUMENT NUMBER: 123:246865

TITLE: Peptide-bile acid conjugates as potent nonopiate analgesics

INVENTOR(S): Ruff, Michael R.; Hill, Joanna M.; Kwart, Lawrence D.; Pert, Candace B.

PATENT ASSIGNEE(S): Advanced Peptides and Biotechnology Sciences, USA

SOURCE: U.S., 10 pp. Cont. of U.S. Ser.No.850,141,abandoned.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5446026	A	19950829	US 1993-19830	19930219
PRIORITY APPLN. INFO.:			US 1989-391272	19890809
			US 1990-541199	19900611
			US 1992-850141	19920312

OTHER SOURCE(S): MARPAT 123:246865

AB Cholic, chenodeoxycholic, and deoxycholic acid derivs. of a calcitonin-derived peptide having the sequence Pro-Arg-Thr-Asn-Thr-Gly-Ser-Gly-Thr-Pro-amide are useful in inducing analgesia without behavioral, motor, or neurol. side effects. The compds. also do not enhance Ca<sup>2+</sup> uptake into bone.

IT **169202-47-5 169202-48-6 169202-49-7**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(peptide-bile acid conjugates as potent nonopiate analgesics)

L21 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 21 Sep 1995

ACCESSION NUMBER: 1995:805358 CAPLUS

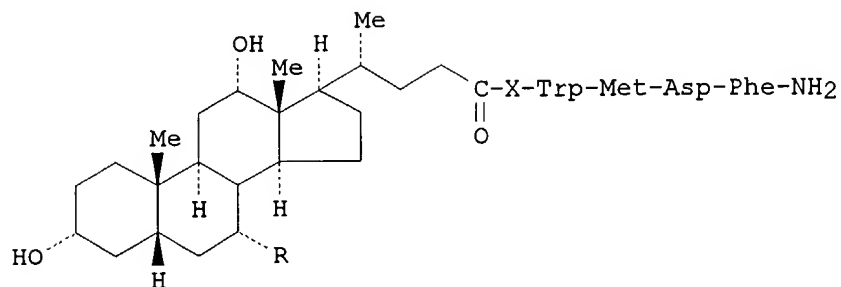
DOCUMENT NUMBER: 124:30355

TITLE: The synthesis of steroid-oligopeptide

AUTHOR(S): Zhang, Xiao; Weng, Ling Ling; Zheng, Hu

10/088807

CORPORATE SOURCE: Department of Biochemistry, Guangdong Medical  
College, Zhanjiang, 524023, Peop. Rep. China  
SOURCE: Chinese Chemical Letters (1995), 6(8), 663-6  
CODEN: CCLEE7  
PUBLISHER: Chinese Chemical Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB Six new steroid-oligopeptides I [R = H, OH; X = bon,  $\beta$ -Ala, His(Tos)] were designed and synthesized with active ester method, and their structures were confirmed by spectra and elemental anal. Preliminary study on their bioactivities showed that I [R = H, X = His(Tos)] inhibits acid secretion and the others promote acid secretion. The metabolic time of six title compds. are longer than the pos. control Boc- $\beta$ -Ala-Trp-Met-Asp-Phe-NH<sub>2</sub>.

IT **171511-54-9P 171511-55-0P 171511-58-3P 171511-59-4P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and acid-secreting promoting and inhibiting activities of steroid-oligopeptide conjugates)

L21 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 03 Sep 1994  
ACCESSION NUMBER: 1994:502451 CAPLUS  
DOCUMENT NUMBER: 121:102451  
TITLE: Steroid cyclophanes as artificial receptors  
embedded in synthetic bilayer membranes:  
aggregation behavior and molecular recognition  
AUTHOR(S): Kikuchi, Junichi; Inada, Masahiko; Miura,  
Hideaki; Suehiro, Kazuaki; Hayashida, Osamu;  
Murakami, Yukito  
CORPORATE SOURCE: Inst. Fundam. Res. Org. Chem., Kyushu Univ.,  
Fukuoka, 812, Japan  
SOURCE: Recueil des Travaux Chimiques des Pays-Bas  
(1994), 113(4), 216-21  
CODEN: RTCPA3; ISSN: 0165-0513  
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Two steroid cyclophanes (I and II), having individually L-lysine and L-aspartate residues as connector units interposed between a 1,6,20,25-tetraaza[6.1.6.1]paracyclophane skeleton and 4 cholate moieties, resp., were designed and synthesized. The cationic steroid cyclophane I, having L-lysine residues, binds anionic and nonionic guests very efficiently, while it has no capacity to bind a guest with a pos. charge in aqueous solution. On the other hand, the anionic steroid cyclophane II, bearing L-aspartate residues, shows good binding affinity toward hydrophobic guests in aqueous solution regardless of their charged states. Aggregate morphol. of the cationic and anionic peptide lipids, involving an L-alanine residue interposed between a charged head moiety and a hydrophobic double-chain segment, in the sonicated vesicular state was not perturbed significantly upon formation of hybrid assemblies with the steroid cyclophanes in 2.5 mol%. Even though the anionic bilayer vesicle interacts only weakly with anionic guests, the corresponding hybrid assembly formed with the cationic steroid cyclophane is capable of marked mol. recognition of anionic guests, along with shape-sensitive discrimination, through electrostatic and hydrophobic interactions in aqueous solution. In a similar manner, the cationic bilayer membrane alone is incapable of binding a cationic guest. However, the guest-binding ability is not much enhanced in the presence of the anionic steroid cyclophane. Consequently, the cationic steroid cyclophane can act as an efficient cell-surface receptor model for anionic guests while the anionic steroid cyclophane is not a good receptor model when both are embedded in bilayer membranes.

IT 156842-47-6P 156916-65-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
 RACT (Reactant or reagent)  
 (preparation and hydrogenation of)

IT 156881-79-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and mol. recognition properties of, as artificial  
 membrane receptor)

L21 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 19 Feb 1994

ACCESSION NUMBER: 1994:71925 CAPLUS

DOCUMENT NUMBER: 120:71925

TITLE: Phospholipid interactions of synthetic peptides  
 containing the antigenic HBV pre S (120-145)  
 sequence

AUTHOR(S): Alsina, M. A.; Rabanal, F.; Mestres, C.;  
 Busquets, M. A.; Reig, F.

CORPORATE SOURCE: Dep. Farm., Fac. Farm., Barcelona, 08028, Spain  
 SOURCE: Journal of Colloid and Interface Science (1993),  
 161(2), 310-5

CODEN: JCISA5; ISSN: 0021-9797

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three lipopeptides derived from HBV-pre S (120-145) sequence containing Stearoyl, Cholanoyl, and Pam3 Cys (Ser)2 moieties were studied as far as their interactions with phospholipids are concerned. The parent compound and the three analogs have surface activity and

penetrate lipid monolayers composed of DPPC; the miscibility of these peptides with the same phospholipid was nearly ideal. The area mol. values calculated for the parent peptide suggest an  $\alpha$ -helical structure and the predicted secondary structure for this sequence, determined by the Chou and Fasman parameters, is also consistent with this conformation. The lipophilic derivs. show, nevertheless, higher mol. areas that fit better with an  $\alpha$  helix and  $\beta$ -sheet segments linked by a  $\beta$  turn. The Pam3 Cys (Ser)2 derivative showed anomalous behavior both in HPLC and in monolayer expts.; probably the bulkiness of the hydrophobic moiety gives preferentially a micellar organization.

IT 134505-87-6

RL: BIOL (Biological study)  
(phospholipid membranes interactions with, antigenic pre S peptide sequence of human hepatitis B virus in relation to)

L21 ANSWER 18 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 13 Nov 1993

ACCESSION NUMBER: 1993:610476 CAPLUS

DOCUMENT NUMBER: 119:210476

TITLE: Cholic and deoxycholic acid conjugates  
containing glycylglycine and alanyl glycine as  
biosurfactants

AUTHOR(S): Tripathi, Meena; Kohli, D. V.; Uppadhyay, R. K.

CORPORATE SOURCE: Dep. Pharm. Sci., Dr. H. G. Gour  
Vishwavidhyalaya, Sagae, India

SOURCE: Pharmazie (1993), 48(7), 552-3  
CODEN: PHARAT; ISSN: 0031-7144

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cholic and deoxycholic acid conjugates with glycylglycine and  
alanyl glycine were prepared and enhanced the solubility and dissoln. of  
poorly water soluble indomethacin and phenylbutazone.

IT 26563-58-6P 103528-73-0P 150698-45-6P

150719-68-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as solubilizer for drugs)

L21 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 13 Nov 1993

ACCESSION NUMBER: 1993:603859 CAPLUS

DOCUMENT NUMBER: 119:203859

TITLE: Preparation of lipid conjugates of therapeutic  
peptides and protease inhibitors

INVENTOR(S): Basava, Channa; Hostetler, Karl Y.

PATENT ASSIGNEE(S): Vical, Inc., USA

SOURCE: PCT Int. Appl., 72 pp.  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9301828	A1	19930204	WO 1992-US6153	19920722

10/088807

W: AU, CA, JP  
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE  
US 5554728 A 19960910 US 1991-734434 19910723  
CA 2113156 AA 19930204 CA 1992-2113156 19920722  
AU 9224251 A1 19930223 AU 1992-24251 19920722  
AU 671078 B2 19960815  
EP 596024 A1 19940511 EP 1992-917096 19920722  
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, MC, NL, SE  
JP 07501316 T2 19950209 JP 1992-503064 19920722  
US 5804552 A 19980908 US 1995-458401 19950602  
PRIORITY APPLN. INFO.: US 1991-734434 19910723  
WO 1992-US6153 19920722

OTHER SOURCE(S): MARPAT 119:203859

AB Title compds., comprising therapeutic peptides, including human immunodeficiency virus (HIV) protease inhibitors covalently linked to phospholipids, glycerides, or other membrane-targeting and membrane-anchoring species, and their pharmaceutically acceptable salts, together with processes for their preps., are described. The invention also provides novel HIV protease inhibitors. The prepared compds. possess useful pharmacol. properties, such as antiviral activity towards viral infection and inhibitory activity towards viral proteases. Therefore, these compds. can be used in the prophylaxis or treatment of viral infections, in particular infections caused by HIV or other retroviruses. The targeting technol. as described for the protease inhibitors is also applicable to a variety of inhibitors of other enzymes. Thus, R-Ala-Ala-D- $\beta$ -Nal-Pip-OMe (I; R = Ac,  $\beta$ -Nal =  $\beta$ -naphthylalanine, Pip = pipecolic acid), prepared by standard solid-phase methods, had IC<sub>50</sub> >100  $\mu$ M in an antiviral assay, while dipalmitoylglycerophosphatidylethanolamine conjugate I [R = (R)-Me(CH<sub>2</sub>)<sub>14</sub>CO<sub>2</sub>CH[CH<sub>2</sub>O<sub>2</sub>C(CH<sub>2</sub>)<sub>14</sub>Me]CH<sub>2</sub>OP(O)(OH)OCH<sub>2</sub>CH<sub>2</sub>NHCOCH<sub>2</sub>CH<sub>2</sub>CO], prepared via coupling of succinylated ethanolamine derivative ROH with the corresponding peptide, had IC<sub>50</sub> = 10  $\mu$ M.

IT 150524-66-6P 150524-67-7P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as viral protease inhibitor)

L21 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 21 Aug 1993

ACCESSION NUMBER: 1993:473053 CAPLUS

DOCUMENT NUMBER: 119:73053

TITLE: Synthesis of chenodeoxycholic acid-amino acid derivatives

AUTHOR(S): Xu, Fang; Ren, Jinzhi; Zhu, Jianhua

CORPORATE SOURCE: Dep. Pharm. Chem., China Pharm. Univ., Nanjing, Peop. Rep. China

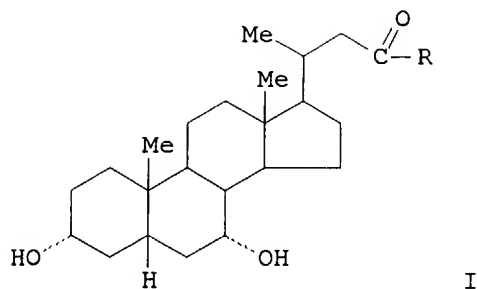
SOURCE: Zhongguo Yaoke Daxue Xuebao (1992), 23(5), 298-300

CODEN: ZHYXE9; ISSN: 1000-5048

DOCUMENT TYPE: Journal

LANGUAGE: Chinese

GI



AB Four novel derivs. I (R = PheOEt, Leu-PheOEt, Val-PheOEt, Sar-TryOEt) of chenodeoxycyloic acid were synthesized by means of the direct condensation of 3 $\alpha$ ,7 $\alpha$ -dihydroxy-5 $\beta$ -cholan-24-oic acid and the PheOEt, Val-PheOEt and Sar-TyrOEt.

IT **148893-70-3P 148893-71-4P 148906-92-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 Jun 1993

ACCESSION NUMBER: 1993:228658 CAPLUS

DOCUMENT NUMBER: 118:228658

TITLE: Miscibility of HBV peptides and dipalmitoylphosphatidylcholine in monolayers

AUTHOR(S): Alsina, M. A.; Mestres, C.; Rabanal, F.; Busquets, M. A.; Reig, F.

CORPORATE SOURCE: Fac. Farm., Univ. Barcelona, Barcelona, 08028, Spain

SOURCE: Langmuir (1993), 9(4), 1129-33

CODEN: LANGD5; ISSN: 0743-7463

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Three lipopeptides derived from hepatitis B virus (HBV)-S protein (139-148) sequence containing stearyl, cholanoyl, and Pam3Cys(Ser)2 moieties were studied as far as their interactions with phospholipids are concerned. The parent compound and the three analogs have surface activity and penetrate lipid monolayers composed of DPPC. The miscibility of these peptides with the same phospholipid was nearly ideal. The area mol. values calculated for the parent peptide suggest an  $\alpha$ -helical structure and the predicted secondary structure for this sequence, determined by the Chou and Fasman parameters, is also consistent with this conformation. The lipophilic derivs. show, nevertheless, higher mol. areas that fit better with an  $\alpha$ -helix and  $\beta$ -sheet segments linked by a  $\beta$ -turn. The Pam3Cys(Ser)2 derivative showed an anomalous behavior both in HPLC and in monolayer expts., probably the bulkiness of the hydrophobic moiety gives preferentially a micellar structure.

IT **134269-14-0**

RL: PRP (Properties)

(miscibility of, with phospholipid in monolayers, surface activity in relation to)

L21 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 30 Mar 1993

ACCESSION NUMBER: 1993:119560 CAPLUS

DOCUMENT NUMBER: 118:119560

TITLE: Tetrapeptide inhibitors of protein  
farnesyltransferase: Amino-terminal  
substitution in phenylalanine-containing  
tetrapeptides restores farnesylation

AUTHOR(S): Brown, Michael S.; Goldstein, Joseph L.; Paris,  
Kenneth J.; Burnier, John P.; Marsters, James  
C., Jr.

CORPORATE SOURCE: Southwest. Med. Cent., Univ. Texas, Dallas, TX,  
75235, USA

SOURCE: Proceedings of the National Academy of Sciences  
of the United States of America (1992), 89(17),  
8313-16

CODEN: PNASA6; ISSN: 0027-8424

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Protein farnesyltransferase from rat brain transfers farnesyl  
residues to cysteine residues in tetrapeptides that conform to the  
sequence CA1A2X, where C is cysteine, A1 and A2 are aliphatic amino  
acids, and X is methionine or serine. When the A2 residue is aromatic  
[e.g., phenylalanine as in Cys-Val-Phe-Met (CVFM)], the tetrapeptide  
continues to bind to the enzyme, but it can no longer accept a  
farnesyl group, and it becomes a pure inhibitor. The current  
studies show that this resistance to farnesylation also requires a  
pos. charge on the cysteine amino group. Derivatization of this  
group with acetyl, octanoyl, or cholic acid residues or extension of  
the peptide with an addnl. amino acid restores the ability of  
phenylalanine-containing peptides to accept a farnesyl residue. The  
same result was obtained when the amino group of cysteine was  
deleted (mercaptopropionyl-VFM). These data suggest that the pos.  
change on the cysteine amino group acts in concert with an aromatic  
residue in the A2 position to render peptides resistant to  
farnesylation by the rat brain enzyme.

IT 146296-43-7

RL: BIOL (Biological study)

(protein farnesyltransferase inhibition by, structure in relation  
to)

L21 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 26 Jul 1992

ACCESSION NUMBER: 1992:423700 CAPLUS

DOCUMENT NUMBER: 117:23700

TITLE: Characterization of the transport of a synthetic  
bile salt, iodinated cholyl-glycyl-tyrosine, in  
isolated cultured rat hepatocytes

AUTHOR(S): Deutsch, John C.; Iwahashi, Mieko M.;  
Sutherland, Eileen M.; Mapoles, John; Simon,  
Francis R.

CORPORATE SOURCE: Sch. Med., Univ. Colorado, Denver, CO, 80262,  
USA

SOURCE: Hepatology (Philadelphia, PA, United States)  
(1992), 15(5), 917-22

CODEN: HPTLD9; ISSN: 0270-9139

DOCUMENT TYPE: Journal

LANGUAGE: English

- AB The uptake of tri-hydroxy conjugated bile salts by hepatocytes is principally by a Na<sup>+</sup>-dependent carrier. The authors examined the uptake kinetics of the high-specific-activity, hydroxylated, conjugated bile salt 125I-labeled cholyl-glycyl-tyrosine, to determine whether this synthetic bile salt was transported by the Na<sup>+</sup>-dependent bile salt system. 125I-labeled cholyl-glycyl-tyrosine was synthesized, and its transport kinetics were studied in freshly cultured rat hepatocytes. Uptake into hepatocytes was time and temperature dependent and was decreased by the inhibitors diisothiocyandisulfonic acid stilbene, probenecid, and carbonyl cyanide chlorophenyl hydrazone, demonstrating carrier mediation and energy dependence. At concns. of iodinated cholyl-glycyl-tyrosine <10  $\mu\text{mol/L}$ , uptake was 27% Na<sup>+</sup> dependent, whereas at concns. of 10-40  $\mu\text{mol/L}$  uptake was 52% Na<sup>+</sup> dependent. The apparent affinity for uptake of 125I-labeled cholyl-glycyl-tyrosine was 8  $\mu\text{mol/L}$ , and the maximal velocity was 50 pmol/ $\mu\text{g}$  DNA/min. Both taurocholate and indocyanine green inhibited uptake of 125I-labeled cholyl-glycyl-tyrosine. Indocyanine green inhibited the uptake of 125I-labeled cholyl-glycyl-tyrosine ( $K_i = 10 \mu\text{M}$ ) more effectively than taurocholate ( $K_i = 20 \mu\text{M}$ ). Thus, 125I-labeled cholyl-glycyl-tyrosine is not a specific probe for either Na<sup>+</sup>-dependent bile salt or Na<sup>+</sup>-independent organic anion carriers, but appears to use both systems in a concentration-dependent manner in cultured rat hepatocytes.
- IT **67319-56-6D**, iodo derivs., iodine-125 labeled  
 RL: BIOL (Biological study)  
 (carrier-mediated transport of, in hepatocyte, kinetics and sodium dependence of)

L21 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 27 Jul 1991

ACCESSION NUMBER: 1991:429883 CAPLUS

DOCUMENT NUMBER: 115:29883

TITLE: Solid phase synthesis of potential antigenic peptides and new lipopeptides of hepatitis B virus

AUTHOR(S): Rabanal, Rancesc; Haro, Isabel; Reig, Francesca; Garica-Anton, Jose M.

CORPORATE SOURCE: Lab. Pep., CID, Barcelona, 08034, Spain

SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1991), (4), 945-52  
 CODEN: JCPRB4; ISSN: 0300-922X

DOCUMENT TYPE: Journal

LANGUAGE: English

- AB Peptides belonging to the envelope protein of hepatitis B virus [Tyr148]S(139-148) R-Cys-Thr-Lys-Pro-Thr-Asp-Gly-Asn-Cys-Tyr-OH [I; R = H, stearyl, cholanoil, R1CO-Cys[CH2CH(CO2R1)CH2O2CR1]-Ser-Ser; R1 = Me(CH2)14], and preS(120-145) R-Met-Glu-Trp-Asn-Ser-Thr-Ala-Leu-His-Gln-Ala-Leu-Gln-Asp-Pro-Arg-Val-Arg-Gly-Leu-Tyr-Leu-Pro-Ala-Gly-Gly-OH (R = same), have been synthesized using the continuous-flow 9-fluorenylmethoxycarbonyl (Fmoc) polyamide solid phase methodol. Benzotriazol-1-yloxytris(pyrrolidino)phosphonium hexafluorophosphate

(PyBOP) and benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP) proved to be convenient reagents to promote the coupling of these lipid moieties to peptides attached to Kieselguhr-supported polyacrylamide resins. Some synthetic aspects concerning reaction conditions and the use of different scavengers at the cleavage stage are discussed. Finally, a cyclic derivative of I (R = H) was obtained through a disulfide bond formation.

IT 134269-14-0P 134505-87-6P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as potential hepatitis B virus antigen)

L21 ANSWER 25 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 15 Jun 1991

ACCESSION NUMBER: 1991:234930 CAPLUS

DOCUMENT NUMBER: 114:234930

TITLE: Effect of cholic and deoxycholic acid conjugates on solubility and dissolution of indomethacin and phenylbutazone

AUTHOR(S): Tripathi, Meena; Kohli, D. V.; Uppadhyay, R. K.  
CORPORATE SOURCE: Dep. Pharm. Sci., Dr. H. S. Gour Vishwavidyalaya Sagar, Sagar, 470 003, India

SOURCE: International Journal of Pharmaceutics (1991), 67(2), 207-9

CODEN: IJPHDE; ISSN: 0378-5173

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The bile acids, cholic acid and deoxycholic acid, were conjugated with the tripeptides, glycylglycylglycine and alanylglycylglycine, to prepare the sodium salts N-[3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-24-oxocholan-24-yl]glycylglycylglycine, N-[3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-24-oxocholan-24-yl]alanylglycylglycine, N-[3 $\alpha$ ,12 $\alpha$ -dihydroxy-24-oxocholan-24-yl]glycylglycylglycine, and N-[3 $\alpha$ ,12 $\alpha$ -dihydroxy-24-oxocholan-24-yl]alanylglycylglycine. The effect of these compds. on the solubility and dissoln. behavior of the poorly water-soluble drugs indomethacin and phenylbutazone was investigated. All the biosurfactants enhanced the dissoln. and solubility of both the drugs in phosphate buffer pH 7.2 at 25°.

IT 98584-71-5 133989-66-9 133989-67-0  
134009-14-6

RL: BIOL (Biological study)  
(dissoln. and solubility of indomethacin and phenylbutazone in relation to)

L21 ANSWER 26 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 18 Mar 1990

ACCESSION NUMBER: 1990:99233 CAPLUS

DOCUMENT NUMBER: 112:99233

TITLE: Characterization of sarcosylsarcosodeoxycholic acid formed during the synthesis of sarcosodeoxycholic acid

AUTHOR(S): Batta, Ashok K.; Salen, Gerald; Shefer, Sarah  
CORPORATE SOURCE: NJ Med. Sch., UMDNJ, Newark, NJ, 07103, USA

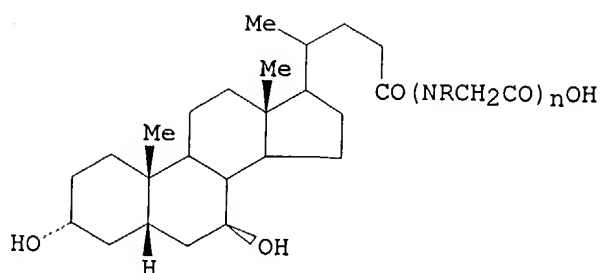
SOURCE: Journal of Lipid Research (1989), 30(5), 771-4

CODEN: JLPRAW; ISSN: 0022-2275

DOCUMENT TYPE: Journal

10/088807

LANGUAGE: English  
GI



AB The peptide derivs. I ( $R = H, Me; n = 2$ ) were obtained as byproducts of I ( $n = 1$ ) when isodeoxycholic acid was treated with  $RNHCH_2CO_2H$ , but not when  $RNHCH_2CO_2Et.HCl$  (II) were used. I ( $n = 2$ ) were obtained in high yield when I ( $n = 1$ ) were treated with II.

IT **125347-55-9P 125347-56-0P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 27 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 03 Sep 1989  
ACCESSION NUMBER: 1989:470314 CAPLUS  
DOCUMENT NUMBER: 111:70314  
TITLE: Lipopeptides as bifunctional inhibitors;  
prevention of elastase-induced emphysema in mice  
by intratracheal pretreatment with  
oleoyl-alanyl-alanyl-prolyl-valine  
AUTHOR(S): Lafuma, C.; Frisdal, E.; Robert, L.; Moczar, E.;  
Lefrancier, P.; Hornebeck, W.  
CORPORATE SOURCE: Lab. Biochim. Tissu Conjonctif, CNRS, Creteil,  
94010, Fr.  
SOURCE: Colloque INSERM (1989), 174(Forum Pept., 2nd,  
1988), 321-4  
CODEN: CINMDE; ISSN: 0768-3154  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Several lipopeptides were synthesized and their ability to inhibit human leukocyte elastase (HLE) was investigated. The extent of inhibition of the protease depends upon the nature of the lipid moiety and the amino acid sequence of the peptide. Oleoyl-alanyl-alanyl-prolyl-valine (I) inhibits competitively HLE with a  $K_i = 4 + 10^{-6}M$ ; the aldehyde ( $K_i = 7 + 10^{-8}M$ ) and chloromethylketone ( $K_i$  .apprx.  $10^{-9}M$ ) derivs. are potent inhibitors of HLE. In contrast the amide derivs. lack inhibitory capacity. These compds. bind to elastin by hydrophobic interactions via the fatty acid and it was demonstrated that in vitro elastin pretreatment by these lipopeptides led to a substrate refractory to elastolysis catalyzed by HLE. Emphysema was induced in mice by intratracheal instillation of HLE; Swiss mice were given a single instillation of I (312 nMoles) one h prior to instillation of HLE.

Pretreatment with the lipopeptide prior to elastase instillation protected the animals from development of emphysema.

IT **121275-23-8P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and elastase of human leukocytes response to, structure in relation to)

L21 ANSWER 28 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 26 May 1989

ACCESSION NUMBER: 1989:185790 CAPLUS

DOCUMENT NUMBER: 110:185790

TITLE: Effect of anesthetic agents on bile flow and biliary excretion of 131I-choloylglycyltyrosine in the rat

AUTHOR(S): Mills, C. O.; Freeman, J. F.; Salt, P. J.; Elias, E.

CORPORATE SOURCE: Dep. Med., Queen Elizabeth Hosp., Birmingham, UK  
SOURCE: British Journal of Anaesthesia (1989), 62(3), 311-15

CODEN: BJANAD; ISSN: 0007-0912

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The effects of i.v. anesthetic agents on bile flow and on the biliary excretion of a novel bile acid, [131I]choloylglycyltyrosine (131I-choloylgly.tyr.) were compared in rats. Etomidate 1 mg bolus and 2 mg/h infusion, Althesin 3 mg bolus and 14.5 mg/h infusion and propofol 3.3 mg bolus and 3.3 mg/h were given via a tail vein cannula and pentobarbitone 50 mg/kg was given by the i.p. route. One hour after cannulation of the common bile duct, 131I-choloylgly.tyr. 5 µCi was injected into the jugular vein and bile was collected every 1 min for 10 min. The mean percentage cumulative biliary excretion of 131I-choloylgly.tyr. at the end of 10 min was: propofol group 74.1 (5.2%); Althesin group 82.3 (2.2%); etomidate group 69.4 (17.6%); pentobarbitone group 76.4 (3.2%). Propofol and Althesin were relatively more choleric, causing bile flow rates twice that produced by pentobarbitone. Only Althesin caused a significant increase in biliary excretion of 131I-choloylgly.tyr. relative to that in rats that received pentobarbitone. Bile flow rates for the resp. anesthetic techniques (µL/min/100 g body weight) (mean) were: propofol group 14.1 (1.8); Althesin group 12.5 (1.7); etomidate 8.5 (1.4); pentobarbitone group 7.3 (1.0). There was a marked metabolic acidosis in all rats except in the propofol group, in which normal acid-base status and oxygenation were observed

IT **67319-56-6**

RL: BIOL (Biological study)  
(excretion of, by bile, anesthetics effect on)

L21 ANSWER 29 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 17 Sep 1988

ACCESSION NUMBER: 1988:493443 CAPLUS

DOCUMENT NUMBER: 109:93443

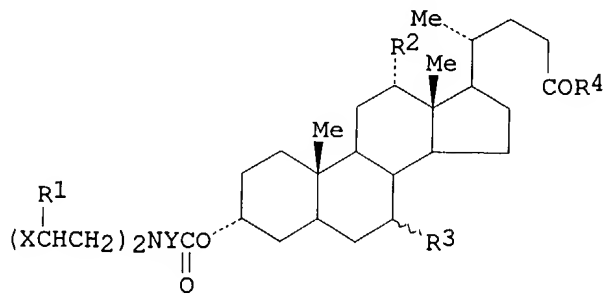
TITLE: Nitrogen mustard derivatives of bile acids for use as carcinostats, and a process for their preparation

INVENTOR(S): Hatono, Shunsou; Yazaki, Akira; Yokomoto,

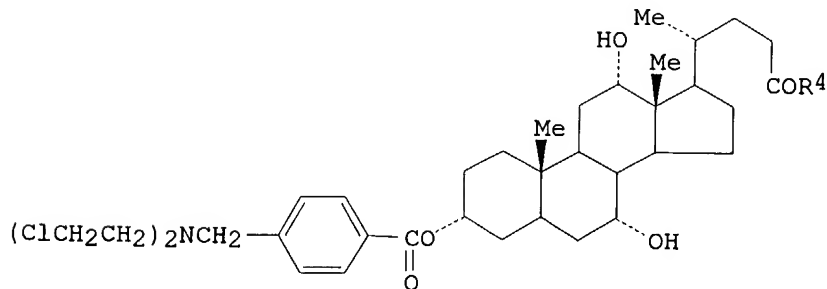
10/088807

PATENT ASSIGNEE(S): Masaharu; Hirao, Yuzo  
 SOURCE: Wakunaga Pharmaceutical Co., Ltd., Japan  
 Eur. Pat. Appl., 26 pp.  
 CODEN: EPXXDW  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 259185	A1	19880309	EP 1987-307846	19870904
R: CH, DE, FR, GB, IT, LI, NL				
JP 63063698	A2	19880322	JP 1986-208901	19860905
US 4810422	A	19890307	US 1987-91957	19870901
PRIORITY APPLN. INFO.:			JP 1986-208901	19860905
OTHER SOURCE(S):			CASREACT 109:93443; MARPAT 109:93443	
GI				



I



II

AB Title derivs. I [R1 = H, alkyl; R2, R3 = H, OH; R4 = OH, alkoxy, OCH2C6H4R5, NH(CH2)mR6; R5 = H, alkoxy; R6 = CO2H, CO2CH2Ph, sulfonyl [i.e., SO3H], or salt thereof; X = halo; Y = (CH2)n, CO2C6H4(CH2)n, (CH2)nC6H4, C6H4(CH2)n; m = 1-4; n = 0-5] are prepared for use as anticancer agents. 4-[(ClCH2CH2)2NCH2]C6H4CO2H was treated with (COCl)2 in CH2Cl2 to give the acid chloride, which was added to a solution of p-methoxybenzyl cholate and pyridine in CH2Cl2 to give 18% [bis(chloroethyl)aminomethylbenzoyl]cholate II (R4 = OCH2C6H4OMe-4). Deprotection of the latter with CF3CO2H and anisole

Searcher : Shears 571-272-2528

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gave 71% II (R4 = OH) (III). At 50  $\mu$ M in vitro, III gave 94% inhibition of 3H-thymidine intake by P388 mouse leukemia cells, vs. 52% by the N mustard Nitromin.

IT **115769-72-7P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of, as carcinostat)

L21 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 23 Jan 1988

ACCESSION NUMBER: 1988:19604 CAPLUS

DOCUMENT NUMBER: 108:19604

TITLE: Ileal absorption of tyrosine-conjugated bile acids in Wistar rats

AUTHOR(S): Mills, Charles O.; Iqbal, Sajida; Elias, Elwyn

CORPORATE SOURCE: Dep. Med., Queen Elizabeth Hosp.,  
Edgbaston/Birmingham, B15 2TH, UK

SOURCE: Biochimica et Biophysica Acta (1987), 926(2),  
154-9

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB 125I-labeled tyrosine- and glycytyrosine-conjugated bile acid or [14C]taurocholate was injected in 400  $\mu$ L aliquots of physiol. saline buffered to pH 7.8 into the ileal lumen of bile-fistula rats. Recovery of bile salts in bile was taken as proof of ileal absorption. In comparison with taurocholate, ileal absorption was .apprx.10% less for cholytyrosine and chenodeoxycholytyrosine and .apprx.50% less for deoxycholytyrosine. Thus, tyrosine-conjugated bile acids are absorbed by the ileum and excreted into bile and may undergo enterohepatic circulation. Low recoveries of deoxycholytyrosine relative to deoxycholyglycine suggested that side chain structure was important for ileal absorption of 3 $\alpha$ ,12 $\alpha$ -dihydroxy bile acids. Elongation of cholic acid to form cholyglycytyrosine markedly reduced 90-min cumulative ileal absorption relative to cholytyrosine. Although initial rates of recovery of cholyglycytyrosine were comparable to those of the other bile acids, very little further absorption was seen in the last hour of the experiment, suggesting that this compound was rapidly degraded within the intestinal lumen.

IT **67319-56-6**

RL: PROC (Process)  
(absorption of, by ileum)

IT **111933-30-3P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 13 Jun 1987

ACCESSION NUMBER: 1987:193422 CAPLUS

DOCUMENT NUMBER: 106:193422

TITLE: Absence of an acinar gradient for bile acid uptake in developing rat liver

AUTHOR(S): Suchy, Frederick J.; Balistreri, William F.;  
Breslin, Joannette S.; Dumaswala, Ranjana;

CORPORATE SOURCE: Setchell, Kenneth D. R.; Garfield, Sanford A.  
Coll. Med., Univ. Cincinnati, Cincinnati, OH,

10/088807

SOURCE: 45267, USA  
Pediatric Research (1987), 21(4), 417-21  
CODEN: PEREBL; ISSN: 0031-3998  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The acinar distribution for uptake of the bile acid analog 125I-labeled cholylglycyltyrosine in livers from adult and 14-day-old suckling rats was studied. Portal and peripheral (systemic) serum bile acid concns. were also measured by combined gas chromatog.-mass spectrometry as an independent index of hepatic bile acid clearance from portal blood. By utilizing light microscopic autoradiog., a steep, decreasing portal to centrilobular gradient for cholylglycyltyrosine uptake was noted in adult rat liver. In contrast, there was no lobular gradient for cholylglycyltyrosine uptake visible in the 14-day-rat liver; all hepatocytes within the acinus contained a similar number of Ag grains. Portal vein total bile acid concns. were higher in serum of adult compared to 14-day-old rats. In contrast, bile acid concns. were 10-fold higher in the peripheral serum of developing vs. adult rats. The peripheral to portal serum bile acid concentration ratio was 0.23 in the adult and 6.48 in the 14-day-old rat. Evidently, the entire hepatic lobule participates in the uptake of bile acids in the 14-day-old rat even under the basal conditions. The normal reserve function of centrilobular hepatocytes is not sufficient to compensate for the decreased transport capacity of the developing liver with the result that increased concns. of bile acids enter and accumulate in the systemic circulation.

IT 108147-75-7

RL: BIOL (Biological study)  
(uptake of, by liver in development, acinar distribution of)

L21 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 06 Sep 1986

ACCESSION NUMBER: 1986:476527 CAPLUS

DOCUMENT NUMBER: 105:76527

TITLE: Synthesis and biliary excretion of

AUTHOR(S): tyrosine-conjugated bile salts in Wistar rats

CORPORATE SOURCE: Mills, Charles O.; Iqbal, Sajida; Elias, Elwyn

Dep. Med., Queen Elizabeth Hosp.,

SOURCE: Edgbaston/Birmingham, B15 2TH, UK

Biochimica et Biophysica Acta (1986), 876(3),

667-76

CODEN: BBACAQ; ISSN: 0006-3002

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Tyrosine-labeled free and glycine-conjugated bile acids were synthesized and radiolabeled with 125I to high purity. The synthetic method utilized excess tyrosine Me ester HCl (1.4 equiv) and bile acid (1 equiv) via DCCD (1.4 equiv) with yields of 90-93% for tyrosine bile acid conjugates and GlyTyr conjugates and 56-60% yields for the GlyGlyTyr conjugates. All of the 8 iodinated tyrosine bile acids tested were rapidly excreted into bile following i.v. injection. In bile duct-cannulated rats with ligated renal pedicles under pentobarbital anesthesia the percentages of injected dose recovered from bile within 20 min were as follows: cholylglycine ([14C]cholylGly), 81.2%; [14C]taurocholate, 94.3%;

Searcher : Shears 571-272-2528

cholylytyrosine (125I-labeled cholylyTyr), 85.5%; 125I-labeled deoxycholylyTyr, 87.9%; 125I-labeled chenodeoxycholylyTyr, 93.4%; 125I-labeled cholylyGlyTyr 95.7%; 125I-labeled deoxycholylyGlyTyr, 92.5%; 125I-labeled chenodeoxycholylyGlyTyr, 94.1%; 125I-labeled cholylyGlyGlyTyr, 85.2%; and 125I-labeled deoxycholylyGlyGlyTyr, 85.5%. Thus, the biliary excretion of 125I-labeled chenodeoxycholylyGlyTyr, chenodeoxycholylyTyr, deoxycholylyGlyTyr, and cholylyGlyTyr was similar to that of [14C]taurocholate, the major naturally occurring bile acid in the rat, and the biliary excretion of all the tyrosine conjugates was similar to or exceeded that of [14C]cholylyGly. Conjugation with tyrosine enhanced the efficiency of plasma-to-bile transport of most naturally occurring bile acids. Comparison of GlyTyr conjugates with GlyGlyTyr conjugates suggests that any addnl. benefit derived by elongation of the side chain is probably negated by obscuring the 12 $\alpha$ -hydroxyl function on the steroid nucleus in the bile acid GlyGlyTyr conjugates.

IT 67319-56-6P 103528-67-2P 103528-68-3P  
103528-69-4P 103528-70-7P 103528-71-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation and bile excretion of)

IT 26563-58-6P 103528-72-9P 103528-73-0P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation and reaction with tyrosine Me ester)

L21 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 01 Jun 1986

ACCESSION NUMBER: 1986:183781 CAPLUS

DOCUMENT NUMBER: 104:183781

TITLE: Pancreatic carboxypeptidase hydrolysis of bile  
acid-amino acid conjugates: selective  
resistance of glycine and taurine amides

AUTHOR(S): Huijghebaert, S. M.; Hofmann, A. F.

CORPORATE SOURCE: Sch. Med., Univ. California, San Diego, La  
Jolla, CA, 92093, USA

SOURCE: Gastroenterology (1986), 90(2), 306-15  
CODEN: GASTAB; ISSN: 0016-5085

DOCUMENT TYPE: Journal

LANGUAGE: English

AB To find a possible explanation for the selective hepatic conjugation of bile acids with glycine or taurine, the N-acyl amides of cholic acid and a number of amino acids and amino acid analogs were synthesized, and their susceptibility to hydrolysis by pancreatic juice, gastric juice, serum, or small intestinal mucosal enzymes was measured. Deconjugation by pure carboxypeptidase A and B was also examined, and hydrolysis by these tissue fluids and enzymes was compared with that mediated by a bacterial cholyglycine hydrolase. Human pancreatic juice efficiently hydrolyzed choly conjugates of all neutral L-amino acids (choly-L-alanine, choly-L-valine, choly-L-leucine, and choly-L-tyrosine), except cholyglycine. The net hourly rate of hydrolysis (in micromoles/mg protein/h) increased when the terminal residue was aromatic or branched aliphatic and appeared to be specific for L- $\alpha$ -amino acids as choly-L-alanine and choly-D-valine were not cleaved. From choly glycyglycine, only the terminal glycine was efficiently removed. Cholytaurine and choly conjugates with the Me and Pr analogs of taurine were

resistant to hydrolysis. Two basic amino acid conjugates (cholyl-L-lysine and cholyl-L-arginine) were cleaved, whereas conjugates of acidic amino acids (cholyl-aspartate and cholyl-cysteate) were not cleaved. Studies with pure enzymes showed that bovine carboxypeptidase A hydrolyzed the cholyl conjugates of the neutral L- $\alpha$ -amino acids with similar specificity as observed for the human pancreatic juice, whereas bovine carboxypeptidase B cleaved the basic amino acid conjugates. Cholyl-L-lysine and cholyl-L-arginine were also cleaved by serum and plasma, which are known to possess carboxypeptidase activity. Cholyl conjugates were not cleaved by gastric juice, trypsin, or homogenates of rat small intestinal mucosa. In contrast, all cholyl conjugates were cleaved by a bacterial cholylglycine hydrolase. Thus, glycine and taurine amides of cholic acid differ from a number of other conjugates with neutral and basic amino acids in being resistant to hydrolysis by pancreatic and plasma carboxypeptidases. These data, together with other data indicating that bile acid conjugation greatly decreases passive intestinal absorption, indicate that a physiologic function of bile acid conjugation with glycine or taurine is to form surfactants that remain indigestible and rather nonabsorbable during digestion in the proximal small intestine.

IT 26563-58-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation and cholylglycine hydrolase hydrolysis of)

L21 ANSWER 34 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 23 Feb 1986

ACCESSION NUMBER: 1986:45877 CAPLUS

DOCUMENT NUMBER: 104:45877

TITLE: Selectively reduced biliary excretion of cholyldiglycylhistamine but not of cholyltetraglycylhistamine in ethinyl estradiol-treated rats. A possible indicator of increased bile canalicular permeability

AUTHOR(S):

CORPORATE SOURCE:

SOURCE:

DOCUMENT TYPE:

LANGUAGE:

AB Cholylglycylhistamine [61601-56-7], cholyldiglycylhistamine [98584-68-0], cholyltriglycylhistamine [98584-69-1], and cholyltetraglycylhistamine [98584-70-4] were synthesized, radioiodinated, and injected i.v. into rats. The cumulative biliary excretions of the 3 larger compds. after 30 min were similar and amounted to >80% of the administered dose. Biliary excretion of cholylglycylhistamine was <50% of the dose, however, suggesting that it fell below the critical mol. weight threshold for effective biliary retention of such compds. Increased bile canalicular permeability induced by treatment with ethinylestradiol [57-63-6] for 7 days should raise this threshold value, a response reflected in the diminished biliary excretion of cholyldiglycylhistamine but not of cholyltetraglycylhistamine. This was consistent with the theory that ethinylestradiol-induced

cholestasis involved increased permeability of bile canicular tight junctions, permitting efflux of bile components from the caniculus to plasma.

IT **98584-68-0P 98584-69-1P 98584-70-4P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and biliary excretion of)

IT **26563-58-6 98584-71-5 98584-72-6**  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (reaction of, with histamine)

L21 ANSWER 35 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
 ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1984:100527 CAPLUS

DOCUMENT NUMBER: 100:100527

TITLE: Intracellular bile acid transport in rat liver  
 as visualized by electron microscope  
 autoradiography using a bile acid analog

AUTHOR(S): Suchy, F. J.; Balistreri, W. F.; Hung, J.;  
 Miller, P.; Garfield, S. A.

CORPORATE SOURCE: Coll. Med., Univ. Cincinnati, Cincinnati, OH,  
 45267, USA

SOURCE: American Journal of Physiology (1983), 245(5,  
 Pt. 1), G681-G689

CODEN: AJPHAP; ISSN: 0002-9513

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **125I**-labeled cholyglycyltyrosine (I), which retains a net neg. charge, exhibited transport properties in rats similar to those of native bile acids. After portal vein injection, the compound was recovered intact from bile, and the pattern of excretion paralleled that of [<sup>14</sup>C]cholyglycine. In addition, I uptake by isolated hepatocytes was Na dependent. For autoradiog., I was injected into the portal vein, and the liver was perfusion fixed after 30 or 300 s. Light microscope autoradiog. performed 30 s after isotope injection demonstrated a steep periportal-to-centrilobular gradient for I uptake. At 30 s, quant. grain anal. of electron microscope autoradiographs showed predominant labeling of the plasma membrane and the smooth endoplasmic reticulum (SER). The grain distribution over the region of the plasma membrane decreased from 15% at 30 s to 7% by 300 s and was associated with a 7-fold increase in labeling of the pericanalicular region. Grain distribution over the SER at 300 s was the same as that noted at 30 s. Thus, bile acids may move from the sinusoidal plasma membrane to bile via a pathway that includes the SER and Golgi apparatus

IT **76763-11-6P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of)

IT **67319-56-6P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation of and hepatocyte intracellular transport pathway for)

L21 ANSWER 36 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
 ED Entered STN: 12 May 1984

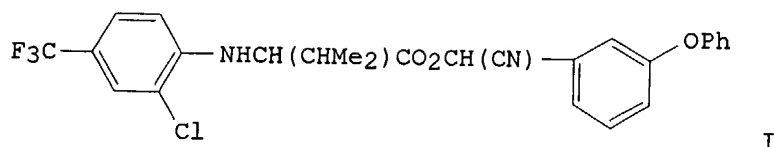
ACCESSION NUMBER: 1982:505275 CAPLUS

DOCUMENT NUMBER: 97:105275

TITLE: Metabolism of fluvalinate by a lactating dairy

10/088807

AUTHOR(S): COW  
Quistad, Gary B.; Staiger, Luana E.; Jamieson,  
Gene C.; Schooley, David A.  
CORPORATE SOURCE: Biochem. Dep., Zoecon Corp., Palo Alto, CA,  
94304, USA  
SOURCE: Journal of Agricultural and Food Chemistry  
(1982), 30(5), 895-901  
CODEN: JAFCAU; ISSN: 0021-8561  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
GI



AB When a lactating cow was given a single oral dose (1 mg/kg) of trifluoromethyl-14C-labeled fluvalinate (I) [69409-94-5], 53, 42, and 0.9% of the applied dose were excreted in urine, feces, and milk, resp., after 8 days. The major urinary metabolites consisted of the anilino acid [76338-73-3], which arose from hydrolysis of I and  $\beta$ -glucuronide conjugate of the anilino acid [82186-95-6], representing 6-19 and 63-76% of the urinary 14C, resp. Fecal 14C-labeled residues consisted of I, the anilino acid, and the bile acid conjugates of the anilino acid, which were present as 47, .apprx.11, and .apprx.13% of the fecal 14C. Although tissues, in general, contained only traces of radiolabel, I contributed .apprx.70% of the 14C-labeled residue in milk and fat.

IT 82186-93-4 82390-09-8 82390-10-1  
RL: BIOL (Biological study)  
(as fluvalinate metabolite, in dairy cattle)

L21 ANSWER 37 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 12 May 1984  
ACCESSION NUMBER: 1981:103833 CAPLUS  
DOCUMENT NUMBER: 94:103833  
TITLE: Reagents and method for measuring the level of conjugated bile acids  
INVENTOR(S): Cole, John W.; Cummins, Laurence M.; Green, Billy J.; Hixson, Harry F., Jr.  
PATENT ASSIGNEE(S): Abbott Laboratories, USA  
SOURCE: U.S., 4 pp. Cont.-in-part of U.S. Ser. No. 677,586, abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 2  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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Searcher : Shears 571-272-2528

10/088807

US 4220598	A	19800902	US 1977-851095	19771114
JP 52128215	A2	19771027	JP 1977-39071	19770407
JP 58051000	B4	19831114		
FR 2348494	A1	19771110	FR 1977-11324	19770414
FR 2348494	B1	19830624		
BE 853669	A1	19771017	BE 1977-176779	19770415
US 4264514	A	19810428	US 1980-124387	19800225
PRIORITY APPLN. INFO.:			US 1976-677586	19760416
			US 1977-851095	19771114

AB N-[N-(3-Sulfolithocholyl)glycyl]histamine, N-cholyltyrosine, N-[N-[N-(3-sulfolithocholyl)glycyl]-ε-aminocaproyl]tyramine, and N-(N-cholylglycyl)tyrosine were prepared. These compds. were intermediates in the preparation of immunoassay reagents useful in the determination of total bile acid concentration in patients with hepatobiliary diseases.

IT **67319-56-6P 76763-11-6P**  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 38 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 12 May 1984  
ACCESSION NUMBER: 1980:555866 CAPLUS  
DOCUMENT NUMBER: 93:155866  
TITLE: Purifying iodinated bile acid conjugates  
INVENTOR(S): Spenney, Jerry G.  
PATENT ASSIGNEE(S): United States Veterans Administration, USA  
SOURCE: U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 719,753, abandoned.  
CODEN: USXXAM  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4207308	A	19800610	US 1977-805960	19770613
CA 1102306	A1	19810602	CA 1977-282640	19770713
JP 53034766	A2	19780331	JP 1977-85941	19770718
DE 2732388	A1	19780511	DE 1977-2732388	19770718
CA 1138431	A2	19821228	CA 1981-372841	19810312
PRIORITY APPLN. INFO.:			US 1976-719753	19760902
			US 1977-805960	19770613
			CA 1977-282640	19770713

AB Cationic bile acid conjugates with amino acids are radioiodinated for use in radioimmunoassay of bile salts and in physiol. studies. Cholylglycylhistamine [61601-56-7] was prepared by coupling cholylglycine [475-31-0] with histamine-2HCl [56-92-8]. This was radioiodinated with Na 125I to give cholylglycyl-125I-histamine (I) immunogen preparation immunization schedule, radioimmunoassay procedure, antibody time curve specificity of tracer and antibody, serum concentration measurements, and blood clearance. In rats 80-90% of the radioactivity of I was excreted by the liver and found in the jejunum and ileum.

IT **67319-56-6DP**, iodine-125 labeled

10/088807

RL: PREP (Preparation)  
(preparation of, for radioimmunoassay of bile salts)

L21 ANSWER 39 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 12 May 1984  
ACCESSION NUMBER: 1980:465429 CAPLUS  
DOCUMENT NUMBER: 93:65429  
TITLE: 125I-labeled conjugated cholic acids for  
radioimmunoassay  
INVENTOR(S): Morikawa, Junji; Shiina, Yoshiharu; Osawa,  
Ryuzaburo  
PATENT ASSIGNEE(S): Eiken Chemical Co., Ltd., Japan  
SOURCE: Jpn. Kokai Tokkyo Koho, 3 pp.  
CODEN: JKXXAF  
DOCUMENT TYPE: Patent  
LANGUAGE: Japanese  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 55020453	A2	19800213	JP 1978-93628	19780802

PRIORITY APPLN. INFO.: JP 1978-93628 19780802

AB Glycine or taurine conjugates of cholic acid, chenodeoxycholic acid, deoxycholic acid, ursocholic acid, and lithocholic acid are labeled with 125I as their tyrosine Me esters for use in radioimmunoassay. Thus, glycocholic acid tyrosine Me ester was prepared by the Norman method, and the derivative was labeled with 125I by the chloramine-T method. Blood serum (10 µL), rabbit anti-glycocholic acid antiserum, 125I-labeled compound were mixed and incubated at 4° for 24 h, followed by the addition of goat anti-rabbit γ-globulin antiserum and incubation at 4° for an addnl. 24 h. The reaction mixture was centrifuged at 3000 rpm for 30 min, and the precipitate was counted by a γ-scintillation counter to determine serum glycocholic acid levels. The values ranged 0.45-1.01 nmol/mL for healthy subjects and 3.5-53.8 nmol/mL for patients with liver disease.

IT **74427-77-3**  
RL: ANST (Analytical study)  
(labeling of, with iodine-125, for radioimmunoassay)

L21 ANSWER 40 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
ED Entered STN: 12 May 1984  
ACCESSION NUMBER: 1980:142864 CAPLUS  
DOCUMENT NUMBER: 92:142864  
TITLE: Test for detection and determination of bile  
acids or their conjugates in unextracted serum  
samples  
INVENTOR(S): Miller, Phillip C.  
PATENT ASSIGNEE(S): Abbott Laboratories, USA  
SOURCE: Ger. Offen., 29 pp.  
CODEN: GWXXBX  
DOCUMENT TYPE: Patent  
LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

Searcher : Shears 571-272-2528

10/088807

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2916783	A1	19791031	DE 1979-2916783	19790425
DE 2916783	B2	19810716		
DE 2916783	C3	19820401		
NL 7902396	A	19791030	NL 1979-2396	19790327
AU 7945634	A1	19791101	AU 1979-45634	19790330
AU 527381	B2	19830303		
CA 1093962	A1	19810120	CA 1979-324498	19790330
GB 2020014	A	19791107	GB 1979-11887	19790405
GB 2020014	B2	19821020		
FR 2424536	A1	19791123	FR 1979-10391	19790424
JP 54149700	A2	19791124	JP 1979-49849	19790424
BE 875854	A1	19791025	BE 1979-194838	19790425
SE 7903645	A	19791027	SE 1979-3645	19790425
ES 479985	A1	19800816	ES 1979-479985	19790426
			US 1978-899918	19780426

PRIORITY APPLN. INFO.:  
 AB Immunoassays for detection and determination of bile acids (BAs) and their conjugates in unextd. serum, in which the BAs usually are bound to endogenous protein (i.e., serum albumins) are described. BAs were determined by radioimmunoassay (RIA) using BA-specific antiserum and a buffered reagent containing 0.05 M phosphate, pH 7.5 with 0.9% NaCl, 0.02M Na salicylate, 0.75% bovine  $\gamma$ -globulin, and 0.01% thiomersal. Thus, standard solns. of glycosulfolithocholate (I) were prepared. Iodinated tracer was prepared after coupling histamine to I, labeling with  $^{125}\text{I}$ , and purification by chromatog. on LH-20. Antiserum was obtained in rabbits after immunization with serum albumin-histamine-I conjugates. In the RIA, standard curves were obtained for 0-250 mg I/100 mL. Similarly, glycocholate was determined in unextd. fluids in the presence of barbital buffer.

IT 67319-56-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (preparation and iodination of and antiserum to, for bile acid radioimmunoassay)

L21 ANSWER 41 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN  
 ED Entered STN: 12 May 1984  
 ACCESSION NUMBER: 1979:168979 CAPLUS  
 DOCUMENT NUMBER: 90:168979  
 TITLE: Monoradioiodinated phenolic esters, acids, and amines  
 INVENTOR(S): Akerkar, Anandrao S.; Rutner, Herman  
 PATENT ASSIGNEE(S): Becton, Dickinson and Co., USA  
 SOURCE: U.S., 6 pp.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4120867	A	19781017	US 1976-727407	19760929
US 4202874	A	19800513	US 1978-885447	19780310
US 4310675	A	19820112	US 1979-42009	19790524

Searcher : Shears 571-272-2528

10/088807

PRIORITY APPLN. INFO.:

US 1976-727407

19760929

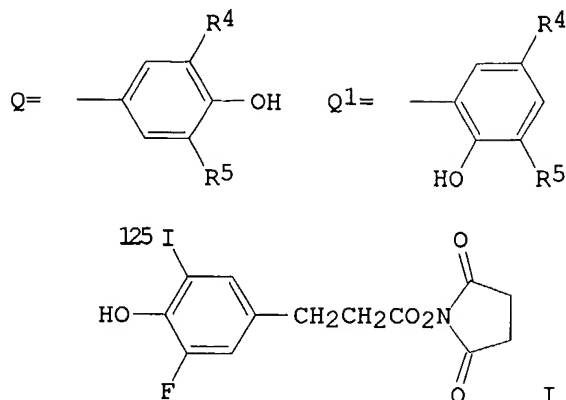
US 1978-885447

19780310

OTHER SOURCE(S):

CASREACT 90:168979

GI



AB RXCO<sub>2</sub>R<sub>1</sub>, RXCH(NHR<sub>2</sub>)CO<sub>2</sub>R<sub>1</sub>, RXNH<sub>2</sub>, and RXCH(NH<sub>2</sub>)CO<sub>2</sub>R<sub>3</sub> (R = Q, Q<sub>1</sub>, R<sub>4</sub>, R<sub>5</sub> = iodine radioisotopes, alkyl, alkoxy, F, Cl, Br, NO<sub>2</sub>; R<sub>1</sub> = H, active ester moiety; R<sub>2</sub> = acyl, PhCH<sub>2</sub>O<sub>2</sub>C; R<sub>3</sub> = H, alkyl, alkali metal, alkaline earth metal; X = Cl-6-alkylene) were prepared. Thus, 3,4-F(HO)C<sub>6</sub>H<sub>3</sub>CH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>H was esterified with N-hydroxysuccinimide by dicyclohexylcarbodiimide and the succinimido ester was radioiodinated with Na<sup>125</sup>I and chloramine-T to give <sup>125</sup>I derivative I, which was treated with TSH (TSH) to give the <sup>125</sup>I acylated TSH. I was used to acylate Ig. Testosterone 3-(O-carboxymethyl)-3-fluoro-3-iodo-<sup>125</sup>-tyrosine Me ester and its aldosterone analog were also prepared.

IT 69889-02-7P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and radioiodination of, with iodine-125)

IT 69889-01-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and saponification of)

IT 69889-03-8P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 42 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1978:503269 CAPLUS

DOCUMENT NUMBER: 89:103269

TITLE: Iodinatable bile salts

INVENTOR(S): Spenney, Jerry Gorton

PATENT ASSIGNEE(S): USA

SOURCE: Ger. Offen., 42 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

Searcher : Shears 571-272-2528

10/088807

LANGUAGE: German  
FAMILY ACC. NUM. COUNT: 3  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 2732388	A1	19780511	DE 1977-2732388	19770718
US 4207308	A	19800610	US 1977-805960	19770613

PRIORITY APPLN. INFO.:  
US 1976-719753 19760902  
US 1977-805960 19770613

AB The preparation of iodinated amino acid derivs. of bile salts is described for use in bile salts radioimmunoassays, hepatic uptake and excretion measurements, and hepatic scintigraphy. Thus, 10 mmol cholyglycine and 10 mmol N-hydroxysuccinimide were dissolved in DMF and 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide-HCl, and the mixture was stirred for 1.5 h at 23°. Then, 10 mmol histamine-HCl and 10 mmol triethylamine were suspended in DMF and added to the activated ester formed. After 2-h reaction, the product, cholyglycyl histamine (I), was isolated by chromatog. on Dowex 50WX8 and crystallized as the HCl salt. Iodination was performed in a reaction mixture containing 50 mmol I, 0.5M phosphate buffer (pH 7.4), and 2 mCi (1 nmol) NaI<sup>125</sup>I in 20% EtOH. A radioimmunoassay is described that uses I<sup>125</sup>I-labeled I. The uses of radioactive I in measuring serum bile salt concns. in blood clearance studies, and in hepatic scintigraphy were also demonstrated.

IT 67319-56-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation);  
RACT (Reactant or reagent)  
(preparation and radioiodination of, radioimmunoassay and scintigraphy in relation to)

L21 ANSWER 43 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1977:73105 CAPLUS

DOCUMENT NUMBER: 86:73105

TITLE: Antibacterial activity of the derivatives of dehydro- and deoxycholic acids

AUTHOR(S): Bellini, A. M.; Vertuani, G.; Cavazzini, G.

CORPORATE SOURCE: Ist. Chim.-Farm. Tossicol., Univ. Ferrara, Ferrara, Italy

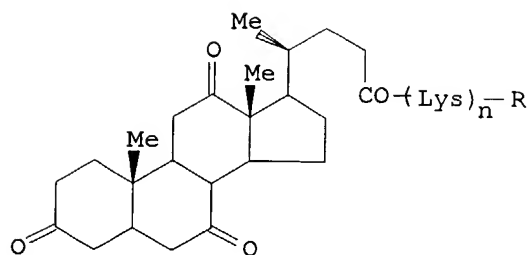
SOURCE: Annali Sclavo (1976), 18(3), 469-78

CODEN: ASCLAZ; ISSN: 0003-472X

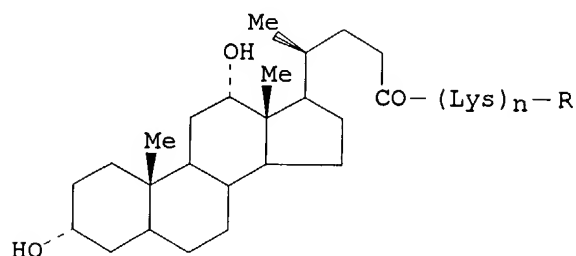
DOCUMENT TYPE: Journal

LANGUAGE: Italian

GI



I



II

AB The title compds. I ( $n = 1$ ,  $R = OH$ ;  $n = 1, 2$ ,  $R = OMe, NH_2$ ) and II ( $n = 1$ ,  $R = OH$ ;  $n = 2$ ,  $R = NH_2$ ) were prepared from the corresponding cholic acids by the mixed anhydride method. I had no bactericidal activity, whereas II were bactericidal against gram-pos. bacteria at 5  $\mu g/ml$  and against gram-neg. ones at 25  $\mu g/ml$ .

IT **61734-74-5P**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and bactericidal activity of)

IT **61761-30-6P**

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(preparation and deblocking of)

L21 ANSWER 44 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1977:73104 CAPLUS

DOCUMENT NUMBER: 86:73104

TITLE: Antibacterial activity of some cholic acid derivatives

AUTHOR(S): Bellini, A. M.; Cavazzini, G.; Vertuani, G.

CORPORATE SOURCE: Ist. Chim.-Farm. Tossicol., Univ. Ferrara, Ferrara, Italy

SOURCE: Annali Sclavo (1976), 18(3), 461-8

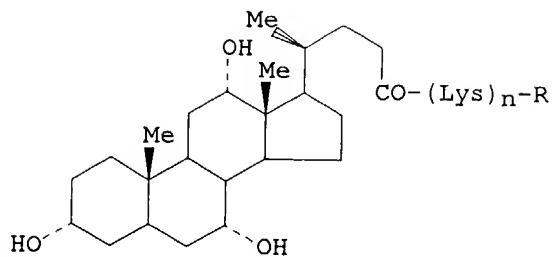
CODEN: ASCLAZ; ISSN: 0003-472X

DOCUMENT TYPE: Journal

LANGUAGE: Italian

GI

10/088807



I

AB Cholyllysine derivs. I ( $n = 1$ ,  $R = OH$ ;  $n = 1,2$ ,  $R = OMe, NH_2$ ) were prepared by the p-nitrophenyl ester and mixed anhydride methods. I ( $n = 1$ ) were bactericidal at 100  $\mu g/ml$  and I ( $n = 2$ ) at 25  $\mu g/ml$ .

IT 61734-76-7P 61734-77-8P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(preparation and bactericidal activity of)

L21 ANSWER 45 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1976:543523 CAPLUS

DOCUMENT NUMBER: 85:143523

TITLE: Cathepsin D inhibitors

INVENTOR(S): Wagner, Arthur Franklin; Holly, Frederick W.;  
Lin, Tsau-Yen; Shen, Tsung-Ying; Hirschmann,  
Ralph F.

PATENT ASSIGNEE(S): Merck and Co., Inc., USA

SOURCE: Ger. Offen., 32 pp.

CODEN: GWXXBX

DOCUMENT TYPE: Patent

LANGUAGE: German

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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DE 2601820	A1	19760722	DE 1976-2601820	19760120
US 3971736	A	19760727	US 1975-542884	19750121
NL 7600165	A	19760723	NL 1976-165	19760108
FR 2298334	A1	19760820	FR 1976-1226	19760119
GB 1489326	A	19771019	GB 1976-2190	19760120
JP 51095062	A2	19760820	JP 1976-5111	19760121
PRIORITY APPLN. INFO.:			US 1975-542884	19750121

AB R1-(X1-Pro-Phe-Phe-Val-X2)n-OH [R1 = H, Me3CO2C, 5-(dimethylamino)-1-naphthalenesulfonyl, D-glucuronyl, cholyl, 2-deoxy-2-acetoamidoglucopyranosyl; X1 = pyroGlu, D-Phe, pyroGlu-D-Phe; X2 = D-Trp, D-Leu, D-Phe, D-Nle, D-Ile;  $n = 1,2,3$ ], useful in doses of 1-15 mg/kg body weight for inhibiting cathepsin D, were prepared by solid-phase method on styrene-divinylbenzene resins. Thus, pyroGlu-D-Phe-Pro-Phe-Phe-Val-D-Trp was prepared by successive coupling of the corresponding tert-butoxycarbonyl blocked amino acids on styrene-divinylbenzene polymers.

Searcher : Shears 571-272-2528

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IT 60667-86-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 46 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1973:84820 CAPLUS

DOCUMENT NUMBER: 78:84820

TITLE: Antibiotic cyclopeptides

PATENT ASSIGNEE(S): Societe des usines chimiques de Rhone-Poulenc

SOURCE: Fr. Addn., 11 pp. Addn. to Fr. M6,878 (CA  
74;88308t).

CODEN: FAXXA3

DOCUMENT TYPE: Patent

LANGUAGE: French

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
	-----	----	-----	-----	-----
	FR 299		19700316	FR 1968-155676	19680619
GI	For diagram(s), see printed CA Issue.				
AB	Cyclopeptides, e.g., I [MeLeu = N-methyl-D-leucine, MePro = trans-4-methylproline, MeThr = N-methylthreonine, MeVal = N-methylvaline [R = 1-dimethylamino-5-naphthylsulfonyl, 11-diethylaminoundecyloxycarbonyl, Et2NCH2CH2O2C, decyloxycarbonyl, p-MeC6H4SO2, protected amino)] (36 compds.) were prepared by substitution on I (R = H). Thus 2 g I.HCl (R = H) was treated with 0.58 g MeSCH2CH2CH(CO2H)NMeCH2Ph in the presence of dicyclohexylcarbodiimide to give 1.31 g I [R = MeSCH2CH2CH(NMeCH2Ph)CO].				

IT 39830-10-9P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(preparation of)

L21 ANSWER 47 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1970:86455 CAPLUS

DOCUMENT NUMBER: 72:86455

TITLE: Purification of glycoconjugates of bile acids by  
ion-exchange chromatography

AUTHOR(S): Setoguchi, Toshiaki

CORPORATE SOURCE: Fac. Med., Kagoshima Univ., Kagoshima, Japan

SOURCE: Acta Medica Universitatis Kagoshimaensis (1969),  
11(2), 117-24

CODEN: AMUKAC; ISSN: 0001-611X

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Crude preps. (Bergstrom and Norman) of glycoconjugated cholic,  
deoxycholic, and lithocholic acids were purified by ion exchange  
chromatog. Similar procedures separated glycine conjugates from  
unconjugated bileacids in human serum and bile.

IT 26563-58-6

RL: ANT (Analyte); ANST (Analytical study)  
(chromatog. of)

10/088807

L21 ANSWER 48 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 12 May 1984

ACCESSION NUMBER: 1969:2361 CAPLUS

DOCUMENT NUMBER: 70:2361

TITLE: Effects of cholic acid-related compounds on experimental hypercholesterolemia and atherosclerosis in rabbits

AUTHOR(S): Aonuma, Shigeru; Mimura, Tsutomu; Mitta, Yukinori; Kadokawa, Toshiaki; Hiramane, Chiharu; Miyai, Kyoko; Saito, Kihachi; Hieda, Tokiko

CORPORATE SOURCE: Fac. Pharm. Sci., Osaka Univ., Osaka, Japan

SOURCE: Yakugaku Kenkyu (1967), 38(12), 409-21

CODEN: YKKKA8; ISSN: 0372-7734

DOCUMENT TYPE: Journal

LANGUAGE: Japanese

AB Chollylleucine, cholytyrosine, cholyglycine, cholyhexaglycine, and cholyldiiodotyrosine lowered the serum total cholesterol/total phospholipids (TC/TP) ratio of cholesterol-fed rabbits. Chollylleucine was the most effective, and completely prevented atherosclerosis in rabbits fed cholesterol for 7 weeks. Cholytyrosine also had prophylactic activity against fatty liver. Cholesterol derivs. did not lower the TC/TP ratio. Serum glucose-6-phosphatase, glutamate-oxalacetate (GOT) and glutamate-pyruvate transaminase (GPT) activities did not change. Cholesterol administration decreased hepatic glucose-6-phosphatase, and choly amino acids did not restore it. Cholesterol administration did not change serum GOT and GPT activities, but chollylleucine and its Et ester markedly increased their serum levels.

IT 22154-47-8

RL: PROC (Process)

(cholesterol in blood serum after administration of)

L21 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2004 ACS on STN

ED Entered STN: 22 Apr 2001

ACCESSION NUMBER: 1965:500804 CAPLUS

DOCUMENT NUMBER: 63:100804

ORIGINAL REFERENCE NO.: 63:18614h,18615a

TITLE: New radioprotective agents; substituted amides of cholic acid

AUTHOR(S): Crippa, G. B.; Bellini, A. M.; Crippa, A.; Rondanelli, E. G.

CORPORATE SOURCE: Univ. Ferrara, Italy

SOURCE: Bollettino Chimico Farmaceutico (1965), 104(8), 479-84

CODEN: BCFAAI; ISSN: 0006-6648

DOCUMENT TYPE: Journal

LANGUAGE: Italian

AB Cysteinecholic acid, cystaminecholamide, cystinecholic acid, homocysteinecholic acid, homocystinecholic acid, and cystaminecholamide were prepared by conjugation of cholic acid with the corresponding  $\alpha$ -amino acids (CA 60, 9351h). Cysteinecholic acid and in a lesser degree cystaminecholamide partially protected proliferating chick embryo megakaryoblasts against x-ray irradiation (800 r.).

IT 5163-93-9, Butyric acid, 4,4'-dithiobis[2-

10/088807

(3 $\alpha$ ,7 $\alpha$ ,12 $\alpha$ -trihydroxy-5 $\beta$ -cholanamido)-  
(in radiation-damage prevention)

E1 THROUGH E98 ASSIGNED

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L22 ANSWER 1 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 220527-56-0 REGISTRY

CN Cholan-24-amide, N,N',N'',N'''-[7,12,22,27-  
tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriaconta-  
3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-  
tetrayltetrakis[(1S)-1-(4-aminobutyl)-2-oxo-2,1-  
ethanediy]]tetrakis[3-hydroxy-, (3 $\alpha$ ,5 $\beta$ )-  
(3' $\alpha$ ,5' $\beta$ )-(3'' $\alpha$ ,5'' $\beta$ )-(3''' $\alpha$ ,5''' $\beta$ )-  
(9CI) (CA INDEX NAME)

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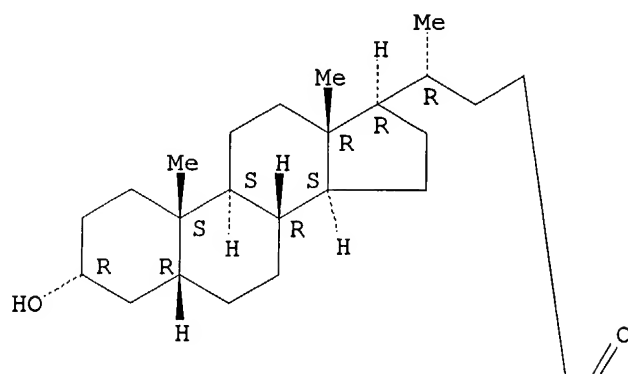
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SR CA  
LC STN Files: CA, CAPLUS  
DT.CA CAplus document type: Conference; Journal  
RL.NP Roles from non-patents: BIOL (Biological study); PREP  
(Preparation); PROC (Process); PRP (Properties)

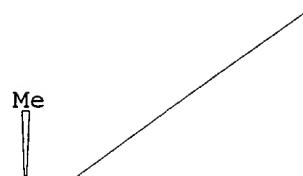
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PAGE 1-A

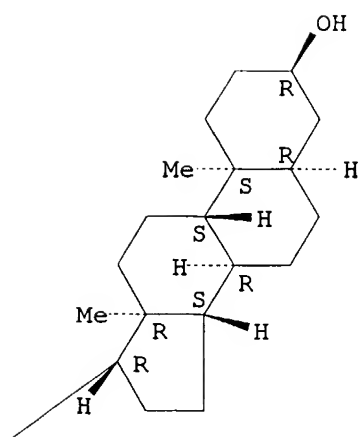


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PAGE 1-B

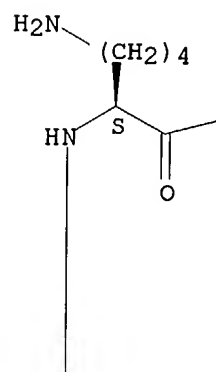
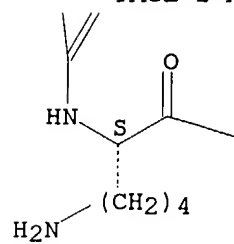


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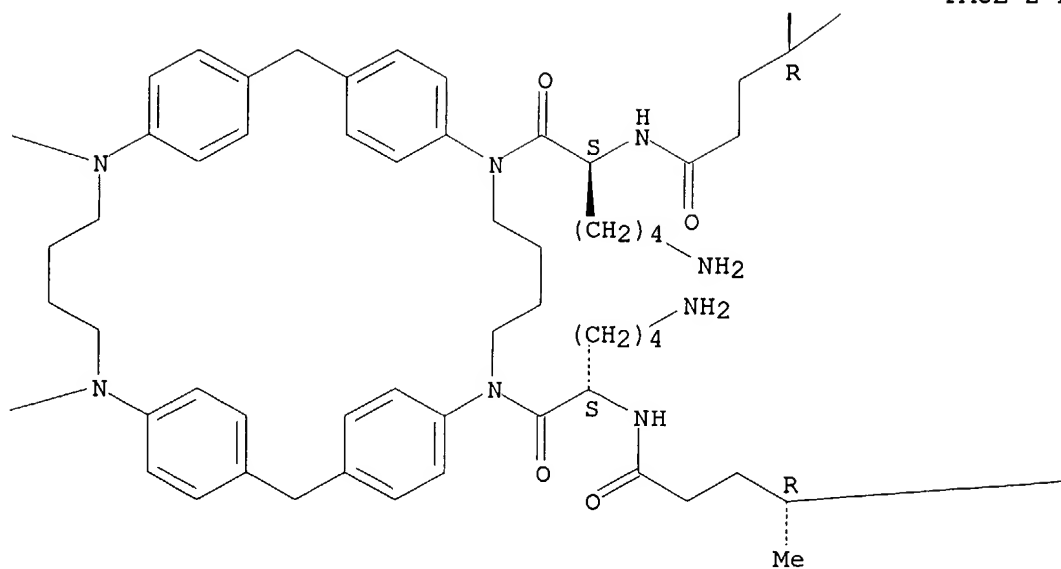


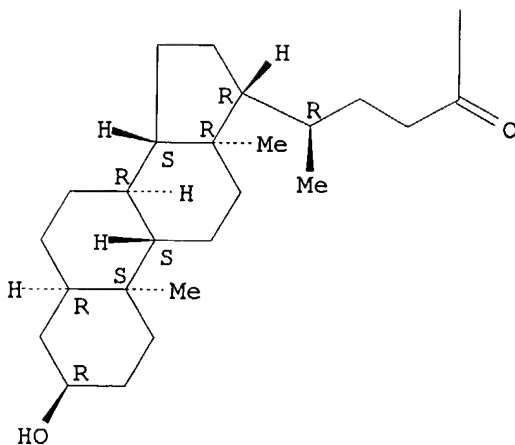
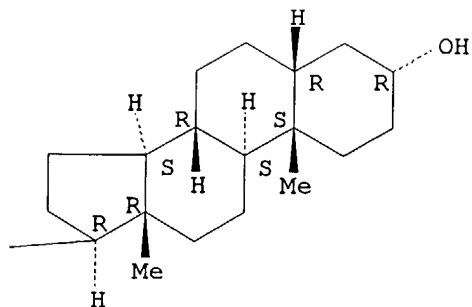
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PAGE 2-A



PAGE 2-B





2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:278125

REFERENCE 2: 130:179092

L22 ANSWER 3 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **208294-95-5** REGISTRY

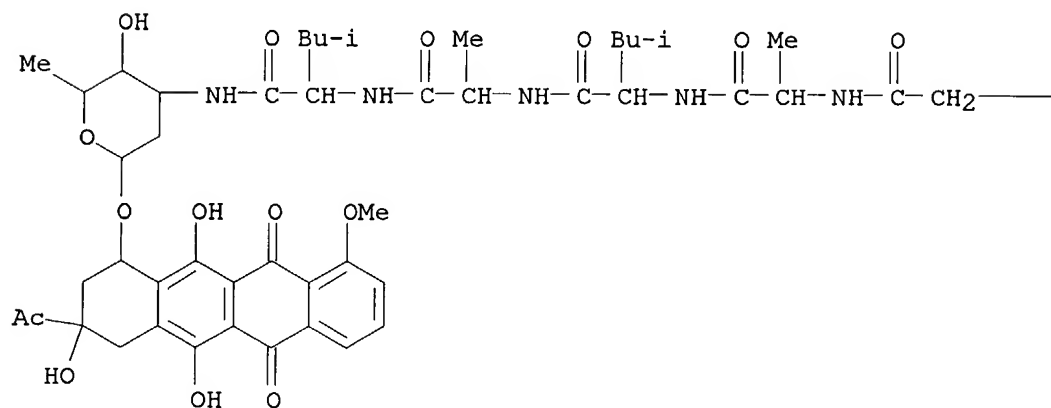
CN 5,12-Naphthacenedione, 8-acetyl-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-10-[[2,3,6-trideoxy-3-[[N-[(3 $\beta$ )-24-oxo-3-[[[(9Z)-1-oxo-9-octadecenyl]oxy]cholan-24-yl]-L-alanyl-L-leucyl-L-

10/088807

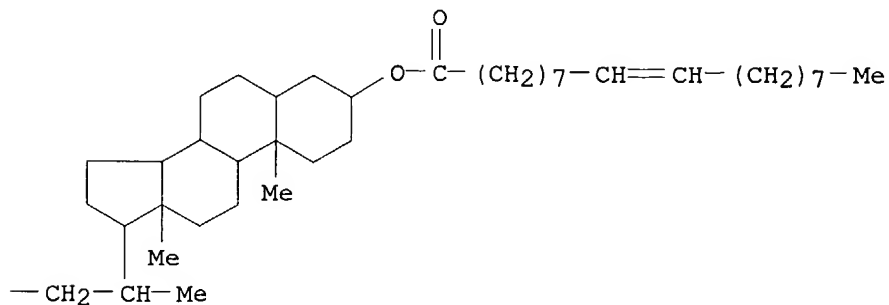
alanyl-L-leucyl]amino]- $\alpha$ -L-lyxo-hexopyranosyl]oxy]-, labeled  
with tritium, (8S,10S)- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE  
MF C87 H131 N5 O17  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER  
DT.CA CAPLUS document type: Journal  
RL.NP Roles from non-patents: BIOL (Biological study); PREP  
(Preparation); PROC (Process)  
IL XH-3

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

PAGE 1-A



PAGE 1-B



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1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 129:45208

L22 ANSWER 4 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 208237-67-6 REGISTRY

CN 5,12-Naphthacenedione, 8-acetyl-7,8,9,10-tetrahydro-6,8,11-trihydroxy-1-methoxy-10-[[[2,3,6-trideoxy-3-[[[N-[(3 $\beta$ )-24-oxo-3-[[[9Z)-1-oxo-9-octadecenyl]oxy]cholan-24-yl]-L-alanyl-L-leucyl-L-alanyl-L-leucyl]amino]- $\alpha$ -L-lyxo-hexopyranosyl]oxy]-, (8S,10S)-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN      LAD

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C87 H131 N5 O17

SR      CA

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA CAplus document type: Journal

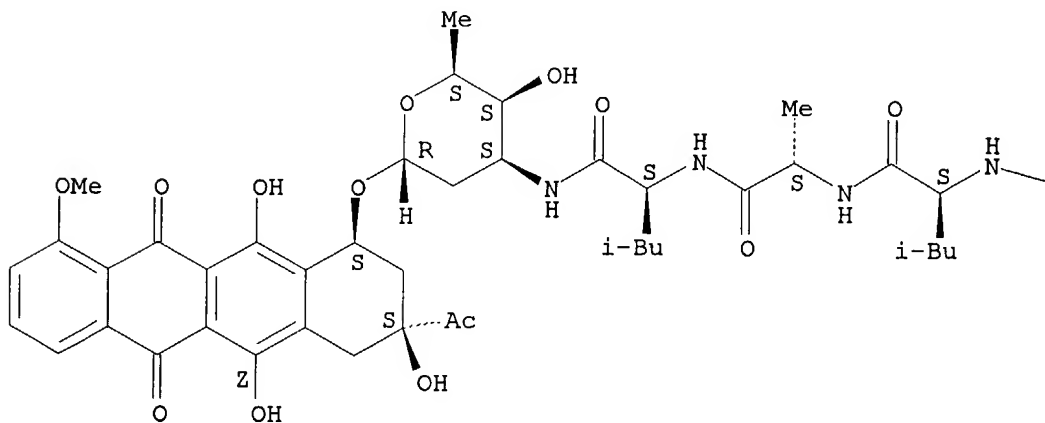
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

\*\*RELATED SEQUENCES AVAILABLE WITH SEOLINK\*\*

Absolute stereochemistry.

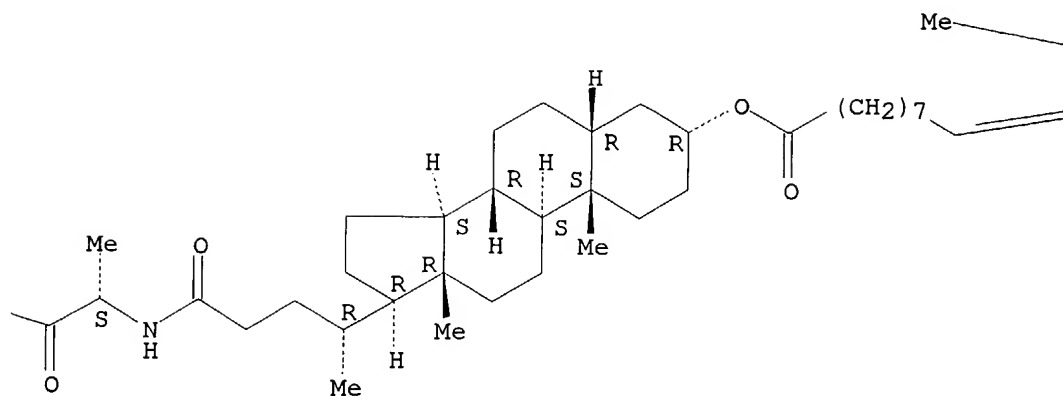
Double bond geometry as shown.

PAGE 1-A

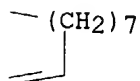


Searcher :        Shears        571-272-2528

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PAGE 1-C



3 REFERENCES IN FILE CA (1907 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:35772

REFERENCE 2: 130:257244

REFERENCE 3: 129:45208

L22 ANSWER 5 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 205588-97-2 REGISTRY

CN L-Proline, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-phenylalanyl-L- $\alpha$ -aspartyl-(9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C42 H61 N3 O10

SR CA

LC STN Files: CA, CAPLUS, TOXCENTER

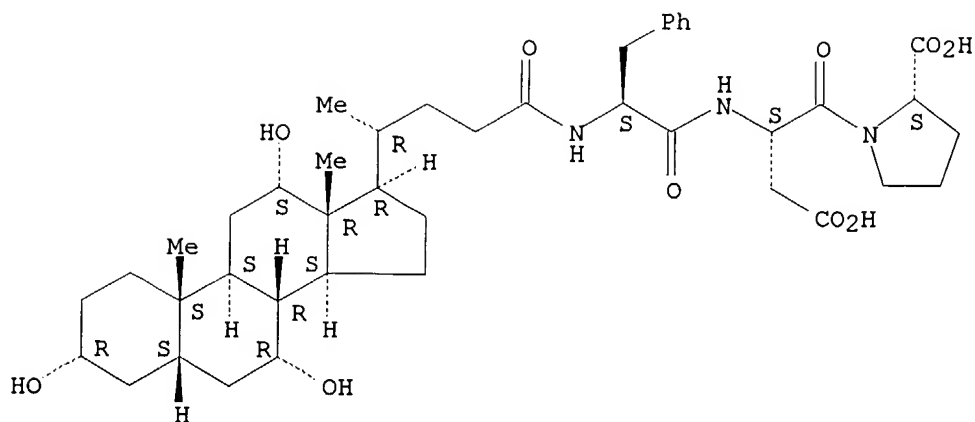
DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: PREP (Preparation)

RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological study); USES (Uses)

Absolute stereochemistry.

10/088807



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

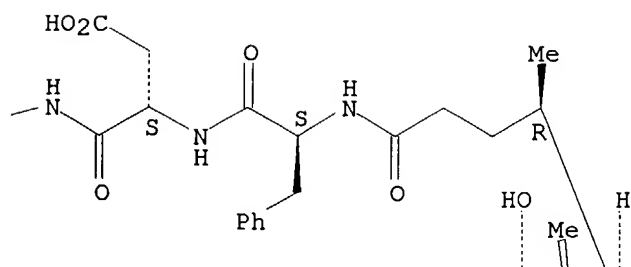
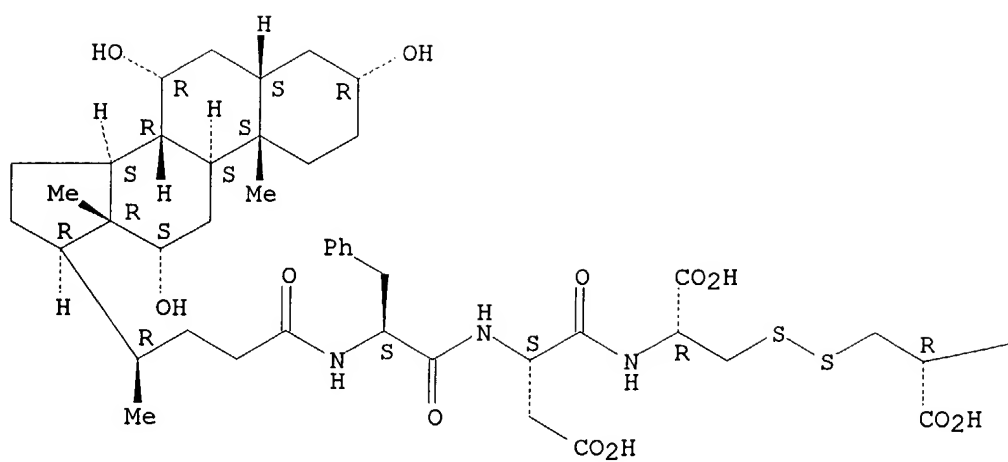
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2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

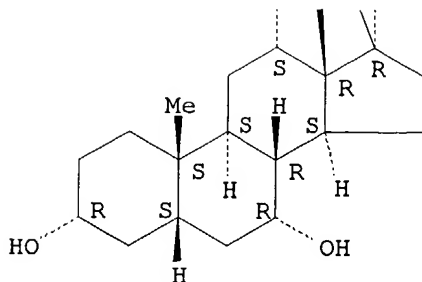
REFERENCE 1: 130:332204

REFERENCE 2: 128:283087

L22 ANSWER 7 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 205587-95-7 REGISTRY  
CN L-Cysteine, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-phenylalanyl-L- $\alpha$ -aspartyl-,  
bimol. (3 $\rightarrow$ 3')-disulfide (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C80 H116 N6 O20 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER  
DT.CA Caplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation);  
USES (Uses)  
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological  
study); USES (Uses)

Absolute stereochemistry.





2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:332204

REFERENCE 2: 128:283087

L22 ANSWER 8 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 205239-05-0 REGISTRY

CN L-Alaninamide, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ,14 $\beta$ )-3,7,12-trihydroxy-23-oxo-24-norcholan-23-yl]-D-alanyl- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C29 H49 N3 O6

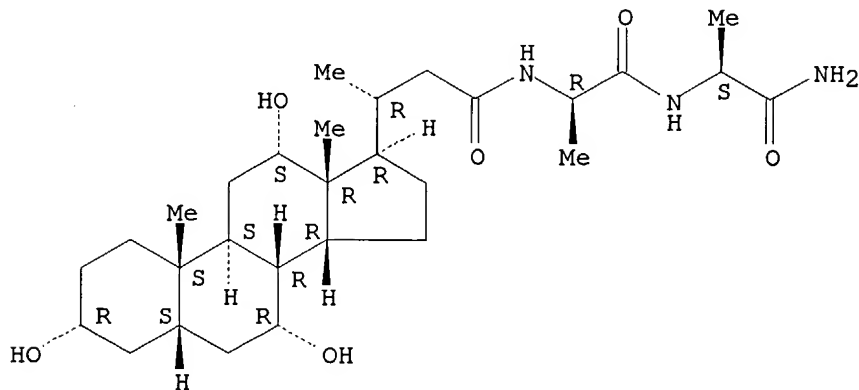
SR CA

LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:254869

L22 ANSWER 9 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **205238-84-2** REGISTRY

CN L-Alaninamide, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ ,14 $\beta$ )-  
3,7,12-trihydroxy-23-oxo-24-norcholan-23-yl]-L- $\alpha$ -glutamyl-L-  
alanyl-L-seryl-L-prolyl-L-seryl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C45 H73 N7 O14

SR CA

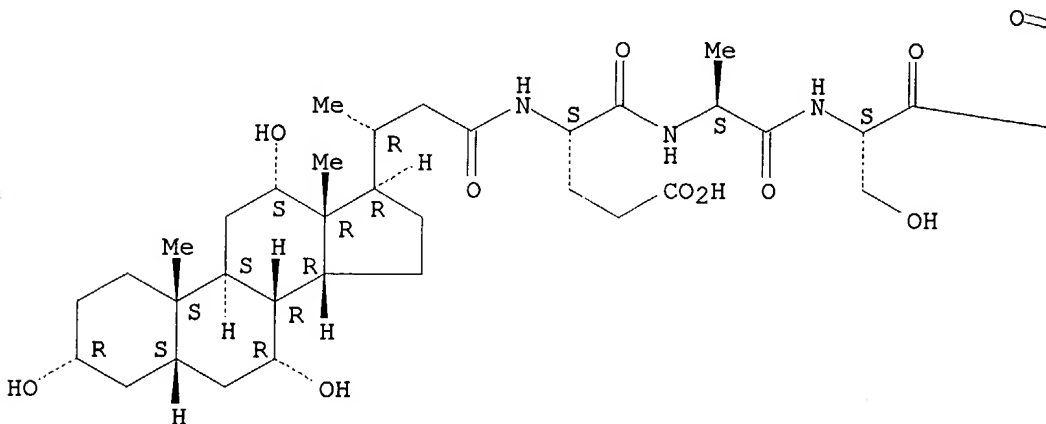
LC STN Files: CA, CAPLUS

DT.CA CAPLUS document type: Journal

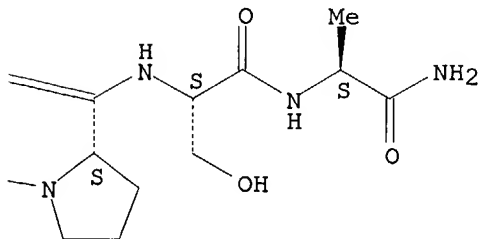
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process)

Absolute stereochemistry.

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1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

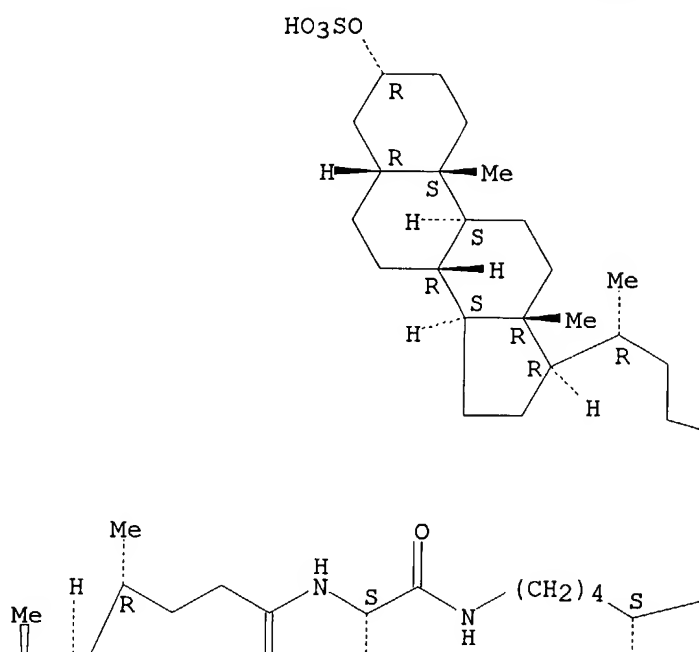
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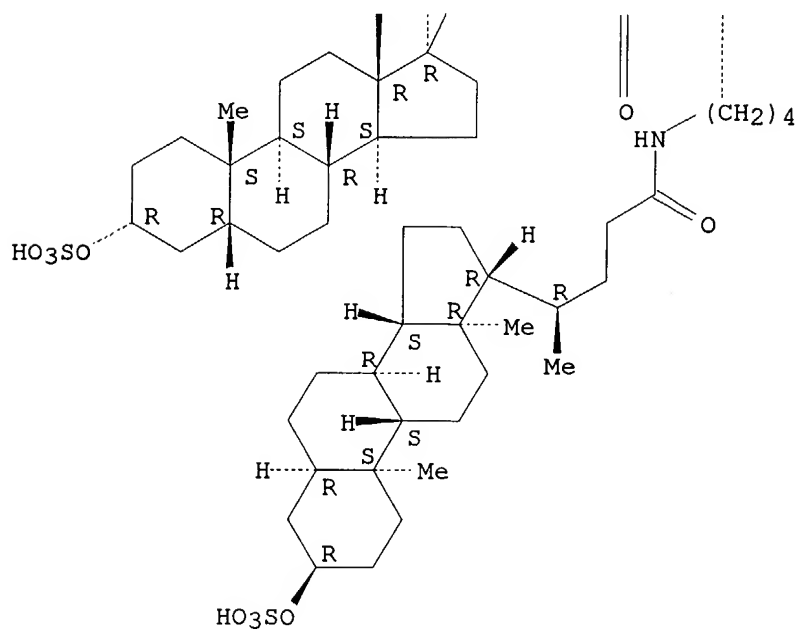
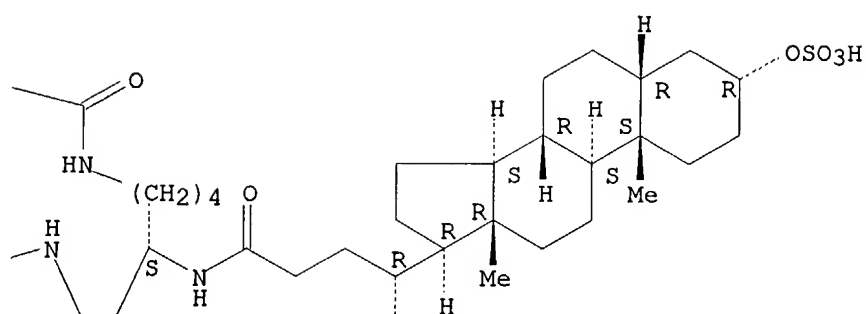
10/088807

L22 ANSWER 19 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **202590-26-9** REGISTRY  
CN L-Lysine, N2,N6-bis[N2,N6-bis[(3 $\alpha$ ,5 $\beta$ )-24-oxo-3-(sulfooxy)cholan-24-yl]-L-lysyl]- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C114 H190 N6 O24 S4  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



CO<sub>2</sub>H

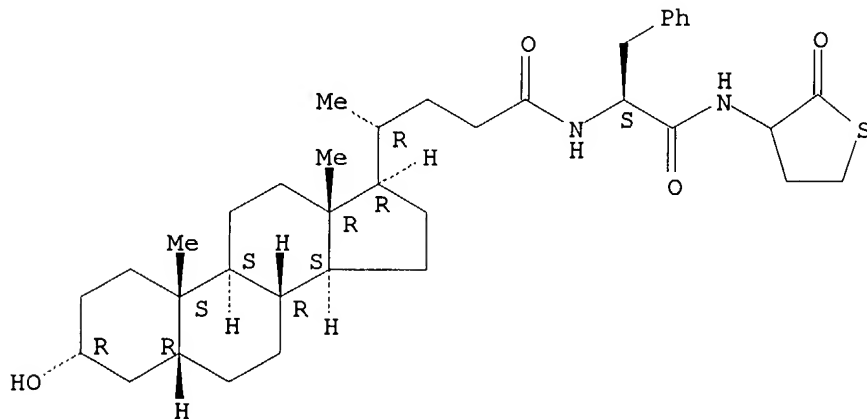


1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 128:154278

L22 ANSWER 24 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **192876-16-7** REGISTRY  
CN Cholan-24-amide, 3-hydroxy-N-[(1S)-2-oxo-1-(phenylmethyl)-2-  
[(tetrahydro-2-oxo-3-thienyl)amino]ethyl]-, (3 $\alpha$ ,5 $\beta$ )-  
(9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C37 H54 N2 O4 S  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL  
DT.CA CAplus document type: Patent  
RL.P Roles from patents: BIOL (Biological study); PREP (Preparation);  
USES (Uses)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:121912

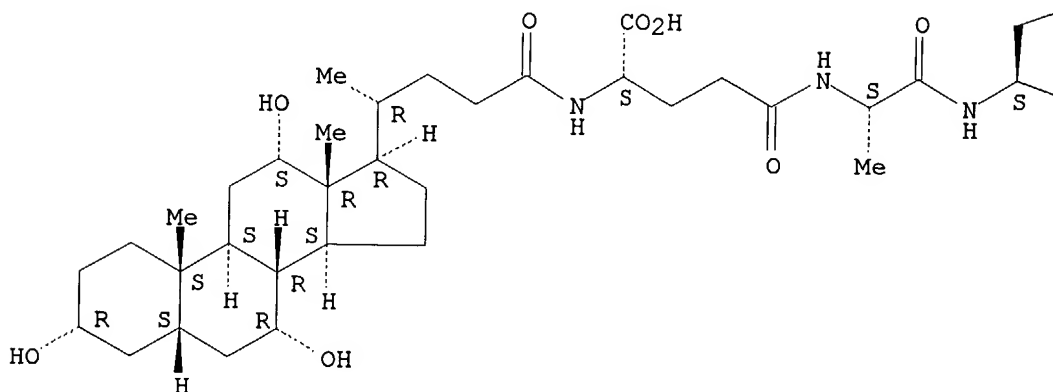
L22 ANSWER 26 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **191528-94-6** REGISTRY  
CN L-Alaninamide, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-  
trihydroxy-24-oxocholan-24-yl]-L- $\gamma$ -glutamyl-L-alanyl-L-seryl-L-

10/088807

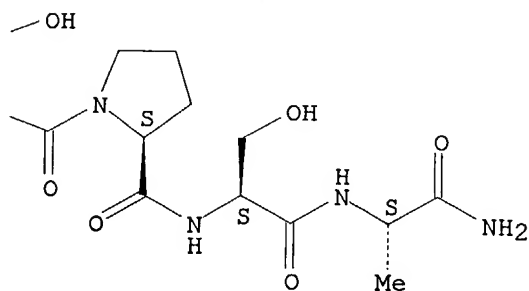
prolyl-L-seryl- (9CI) (CA INDEX NAME)  
FS PROTEIN SEQUENCE; STEREOSEARCH  
MF C46 H75 N7 O14  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA CAPLUS document type: Journal  
RL.NP Roles from non-patents: BIOL (Biological study); PROC (Process)

Absolute stereochemistry.

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 127:70711

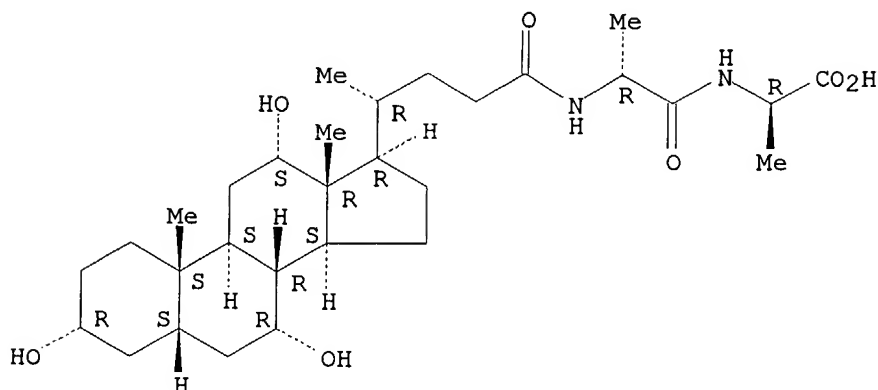
L22 ANSWER 37 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 189261-12-9 REGISTRY  
CN D-Alanine, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-D-alanyl- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C30 H50 N2 O7  
SR CA

Searcher : Shears 571-272-2528

10/088807

LC STN Files: CA, CAPLUS  
DT.CA Caplus document type: Journal  
RL.NP Roles from non-patents: BIOL (Biological study); PREP  
(Preparation); PROC (Process); USES (Uses)

Absolute stereochemistry.



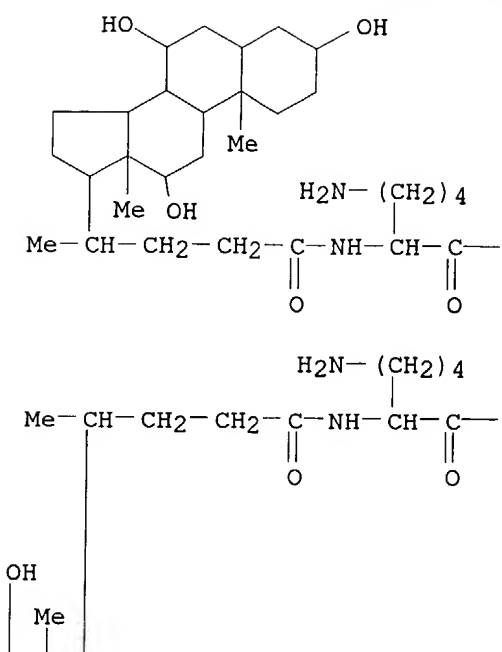
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

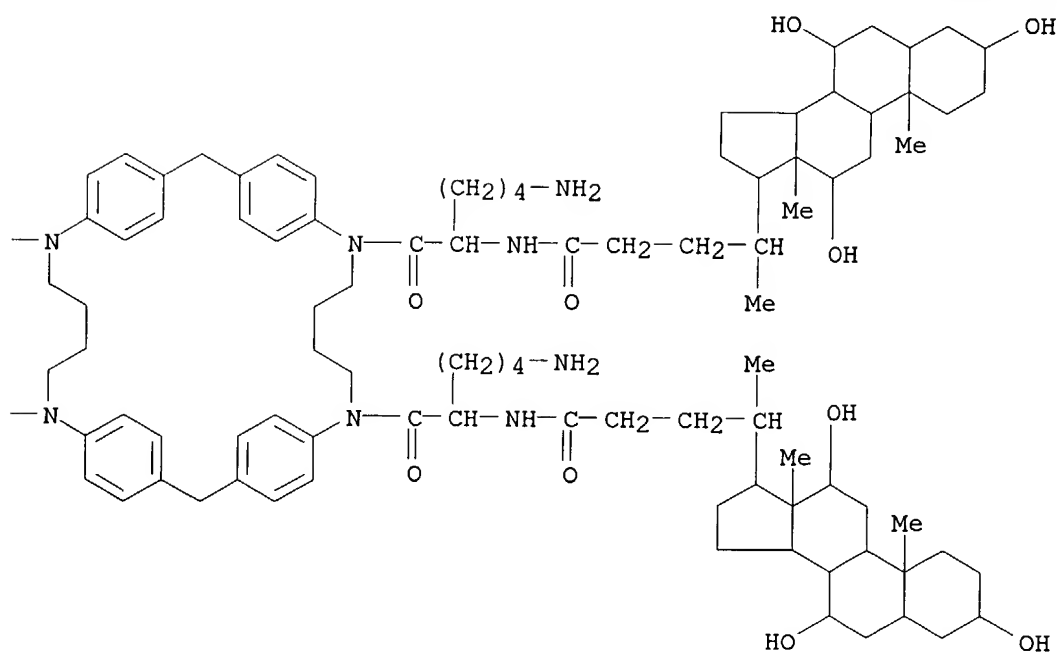
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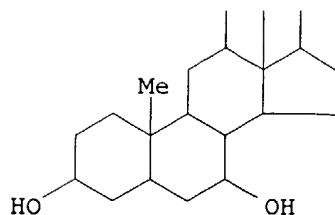
L22 ANSWER 38 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 183072-82-4 REGISTRY  
CN Cholan-24-amide, N,N',N'',N'''-[7,12,22,27-tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-tetrayltetrakis[1-(4-aminobutyl)-2-oxo-2,1-ethanediyl]]tetrakis[3,7,12-trihydroxy-, stereoisomer (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C154 H240 N12 O20  
CI COM  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA Caplus document type: Conference; Journal  
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

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3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:278125

REFERENCE 2: 130:179092

REFERENCE 3: 125:301305

L22 ANSWER 39 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **182889-23-2** REGISTRY

CN Cholan-24-amide, N,N',N'',N'''-[7,12,22,27-tetraazapentacyclo[26.2.2.2.23,6.213,16.218,21]octatriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-tetrayltetrakis[1-(4-aminobutyl)-2-oxo-2,1-ethanediyl]]tetrakis-, stereoisomer (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C154 H240 N12 O8

CI COM

SR CA

LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Conference; Journal

RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties); USES (Uses)

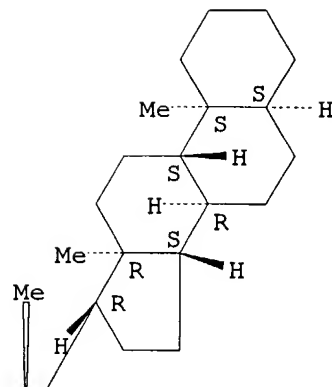
Absolute stereochemistry.

10/088807

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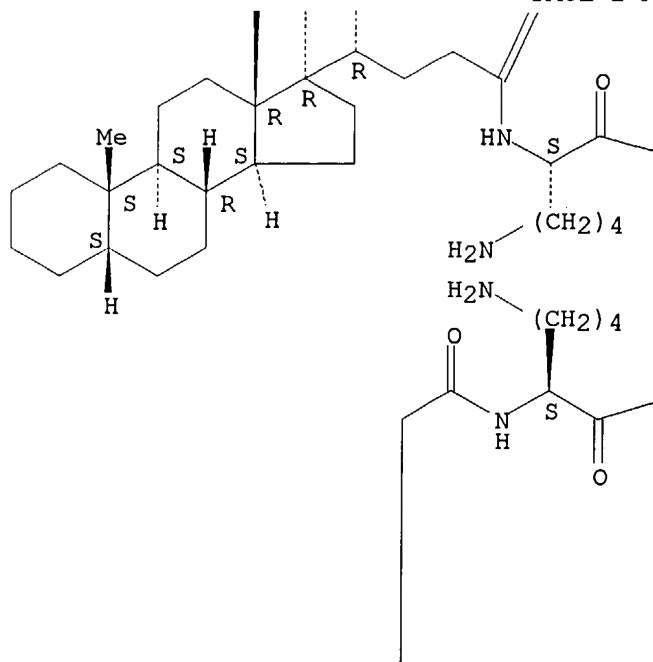


PAGE 1-B

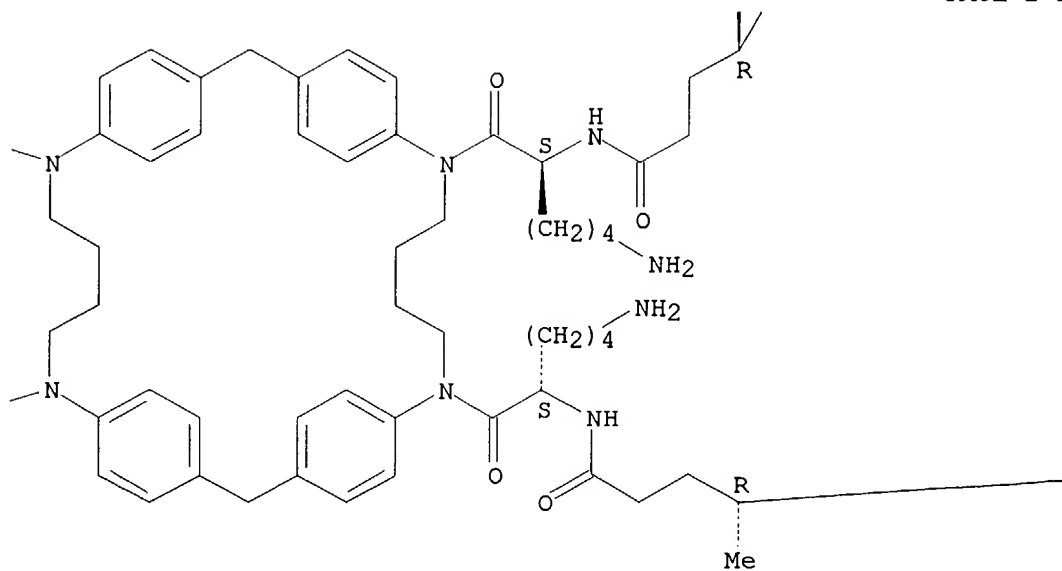


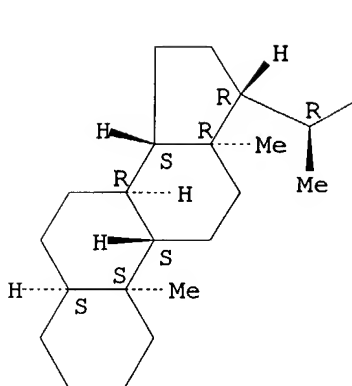
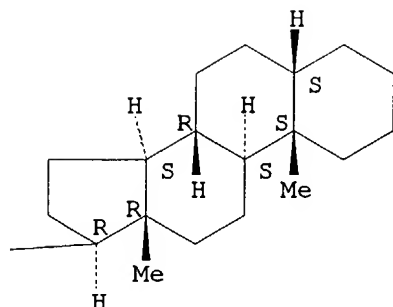
Searcher :        Shears        571-272-2528

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3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:278125

REFERENCE 2: 130:179092

REFERENCE 3: 125:301305

L22 ANSWER 40 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **171511-59-4** REGISTRY

CN 3-7-Cholecystokinin-7 (swine), 3-[N-[(3 $\alpha$ , 5 $\beta$ , 12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-1-[(4-methylphenyl)sulfonyl]-L-histidine]- (9CI) (CA INDEX NAME)

10/088807

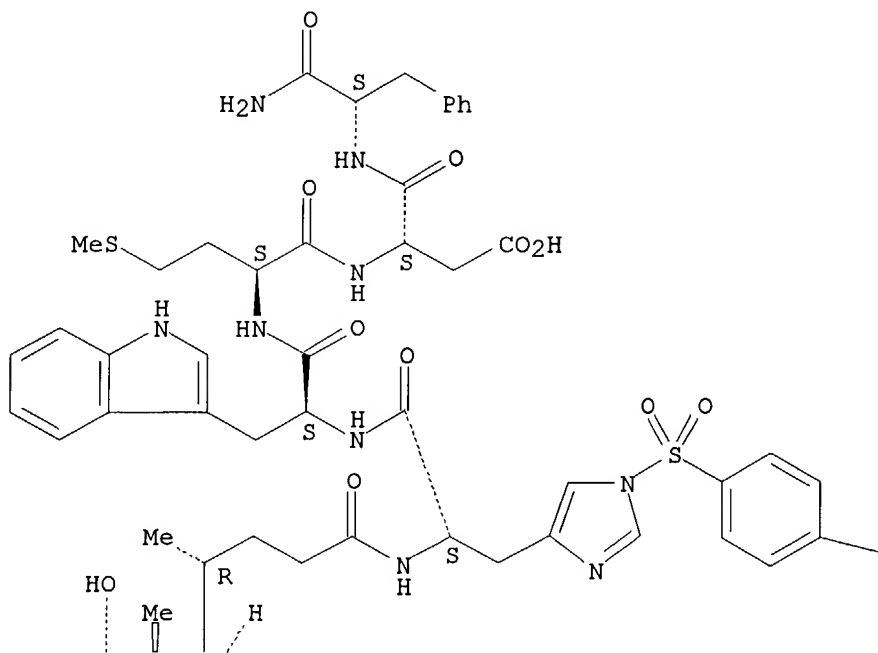
OTHER CA INDEX NAMES:

CN 3-7-Cholecystokinin-7 (pig), 3-[N-[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-1-[(4-methylphenyl)sulfonyl]-L-histidine]-  
FS PROTEIN SEQUENCE; STEREOSEARCH  
MF C66 H87 N9 O12 S2  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA Caplus document type: Journal  
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation)

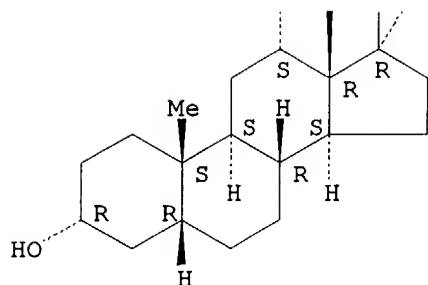
\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

Absolute stereochemistry. Rotation (+).

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Me



2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 126:246641

REFERENCE 2: 124:30355

L22 ANSWER 44 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **169202-49-7** REGISTRY

CN L-Prolinamide, 1-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-prolyl-L-arginyl-L-threonyl-L-asparaginyl-L-threonylglycyl-L-serylglycyl-L-threonyl- (9CI) (CA INDEX NAME)

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C63 H105 N15 O19

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

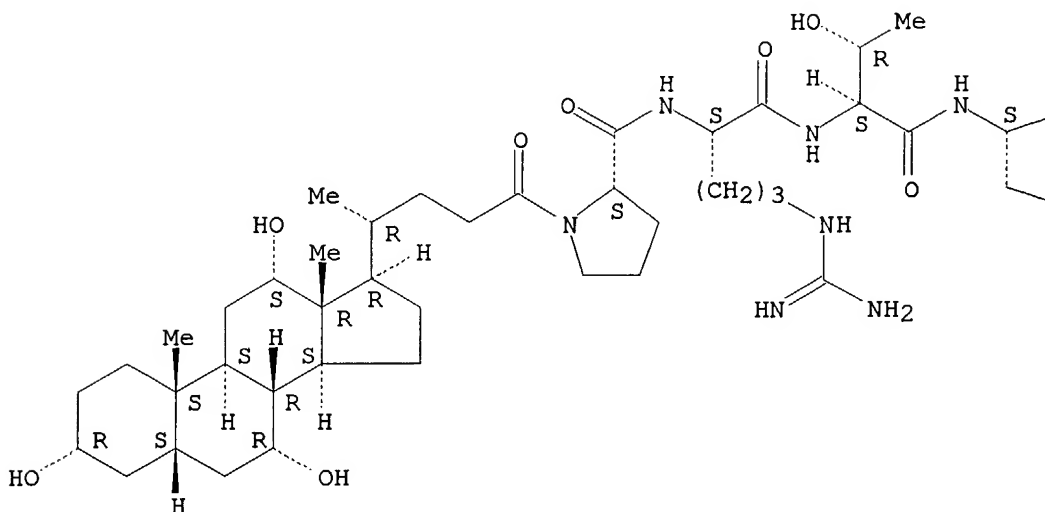
DT.CA CAPLUS document type: Patent

RL.P Roles from patents: BIOL (Biological study); USES (Uses)

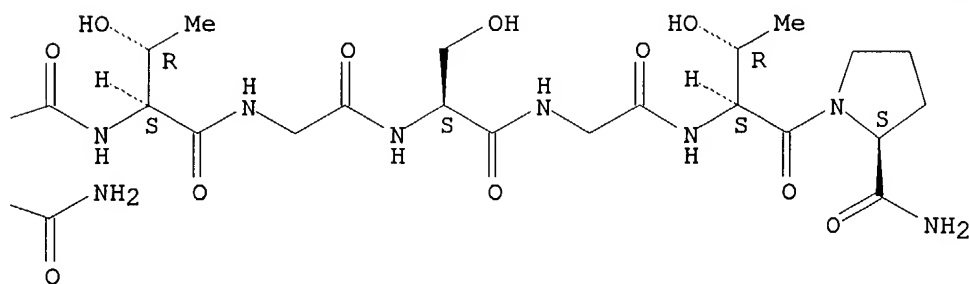
\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 123:246865

L22 ANSWER 47 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 156916-65-3 REGISTRY

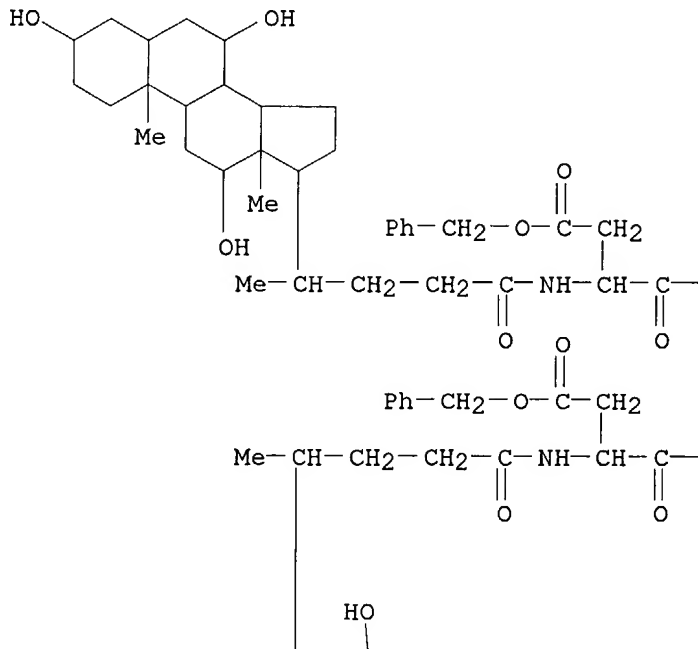
CN 7,12,22,27-Tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriacont  
 a-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-  
 tetrabutanoic acid,  $\gamma,\gamma',\gamma'',\gamma'''$ -tetraoxo-  
 $\beta,\beta',\beta'',\beta'''$ -tetrakis[[(3 $\alpha$ ,5 $\beta$ ,7. $\alpha$ ph  
 a.,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-,

tetrakis(phenylmethyl) ester, ( $\beta$ S, $\beta$ 'S, $\beta$ ''S, $\beta$ '''S)  
 )- (9CI) (CA INDEX NAME)

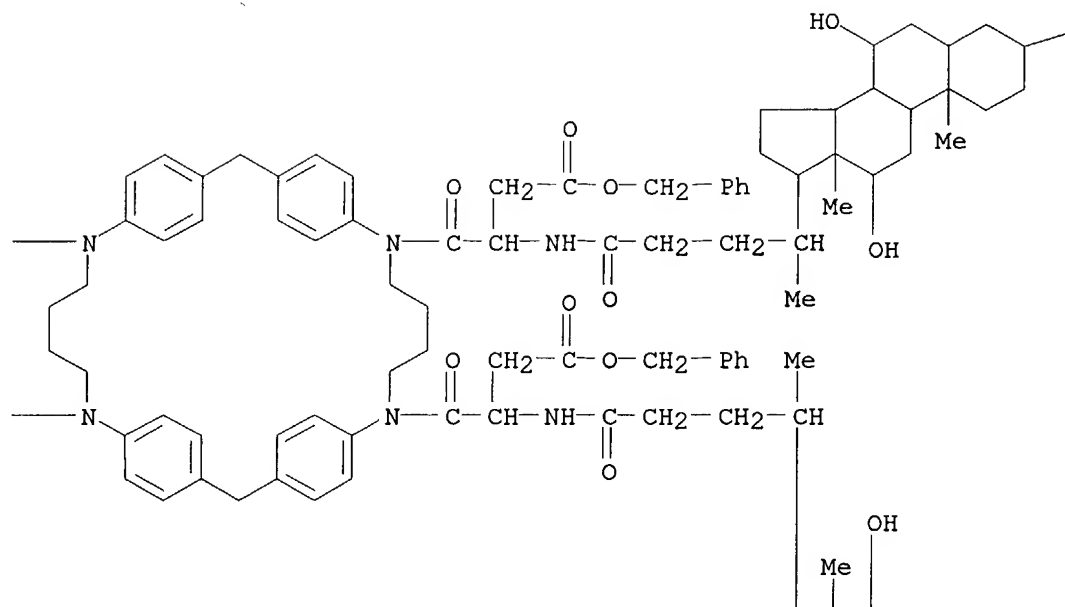
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 tetrabutanoic acid,  $\gamma,\gamma',\gamma'',\gamma'''$ -tetraoxo-  
 $\beta$ - $\beta',\beta'',\beta'''$ -tetrakis[[(3 $\alpha$ ,5 $\beta$ ,7. $\alpha$ ph  
 a.,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-,  
 tetrakis(phenylmethyl) ester, [ $\beta$ S-( $\beta$ R\*, $\beta$ 'R\*, $\beta$ ''R  
 \*, $\beta$ '''R\*)]-  
 FS STEREOSEARCH  
 DR 549480-08-2  
 MF C174 H236 N8 O28  
 CI COM  
 SR CA  
 LC STN Files: CA, CAPLUS  
 DT.CA Caplus document type: Journal  
 RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties);  
 RACT (Reactant or reagent)

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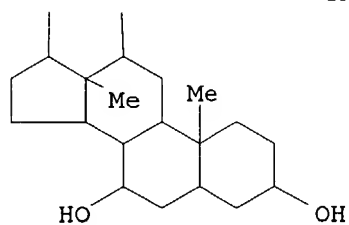
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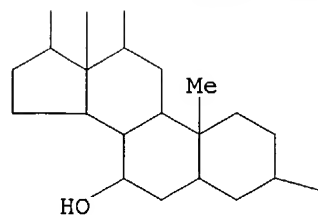
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OH

2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:68909

REFERENCE 2: 121:102451

L22 ANSWER 48 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 156881-79-7 REGISTRY

CN 7,12,22,27-Tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriacont  
a-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-  
tetrabutanoic acid,  $\gamma, \gamma', \gamma'', \gamma'''$ -tetraoxo-  
 $\beta, \beta', \beta'', \beta'''$ -tetrakis[[ (3 $\alpha$ , 5 $\beta$ , 7.alph  
a., 12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-,  
( $\beta$ S,  $\beta'$ S,  $\beta''$ S,  $\beta'''$ S)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 7,12,22,27-Tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriacont  
a-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-  
tetrabutanoic acid,  $\gamma, \gamma', \gamma'', \gamma'''$ -tetraoxo-  
 $\beta, \beta', \beta'', \beta'''$ -tetrakis[[ (3 $\alpha$ , 5 $\beta$ , 7.alph  
a., 12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-,  
[ $\beta$ S-( $\beta$ R\*,  $\beta'$ R\*,  $\beta''$ R\*,  $\beta'''$ R\*)]-

CN Cholane, 7,12,22,27-tetraazapentacyclo[26.2.2.23,6.213,16.218,21]oct  
atriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-  
tetrabutanoic acid deriv.

FS STEREOSEARCH

MF C146 H212 N8 O28

SR CA

LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Journal

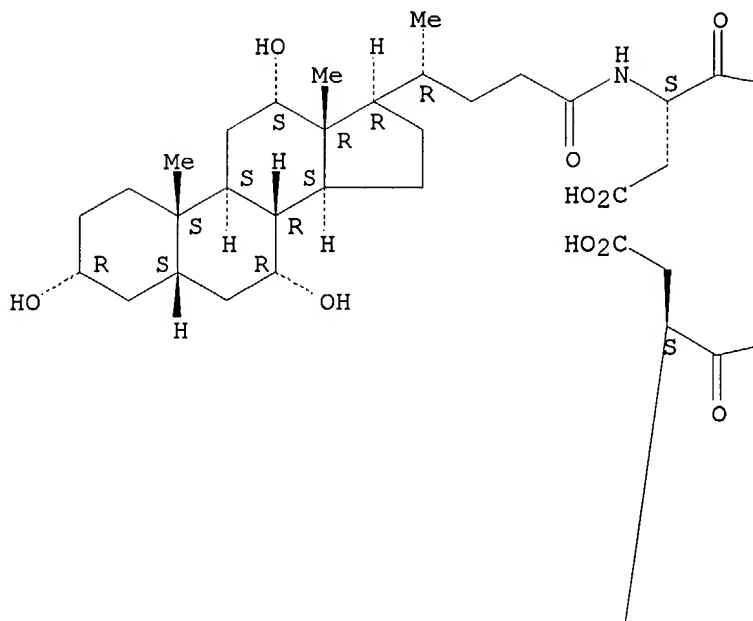
RL.NP Roles from non-patents: BIOL (Biological study); PREP

10/088807

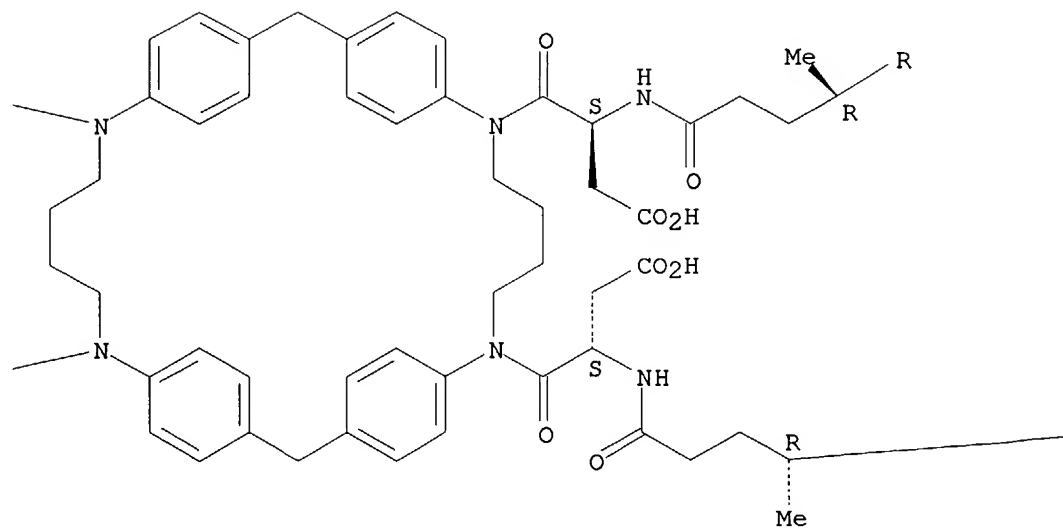
(Preparation); PROC (Process); PRP (Properties)

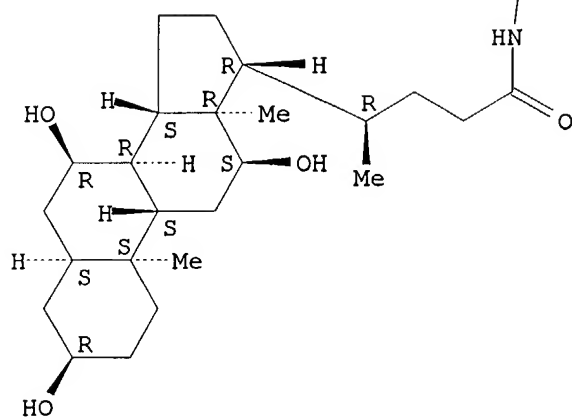
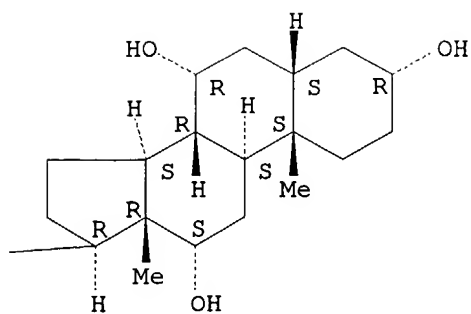
Absolute stereochemistry.

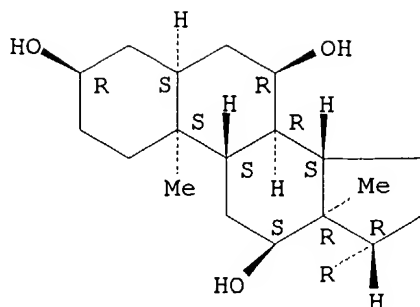
PAGE 1-A



PAGE 1-B







2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 130:179092

REFERENCE 2: 121:102451

L22 ANSWER 49 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **156842-47-6** REGISTRY

CN Carbamic acid, [7,12,22,27-tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-tetrayltetrakis[(5S)-6-oxo-5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-6,1-hexanediyl]]tetrakis-, tetrakis[(2-chlorophenyl)methyl] ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 7,12,22,27-Tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriacontane, carbamic acid deriv.

CN Carbamic acid, [7,12,22,27-tetraazapentacyclo[26.2.2.23,6.213,16.218,21]octatriaconta-3,5,13,15,18,20,28,30,31,33,35,37-dodecaene-7,12,22,27-tetrayltetrakis[6-oxo-5-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]amino]-6,1-hexanediyl]]tetrakis-, tetrakis[(2-chlorophenyl)methyl] ester

CN Cholane, carbamic acid deriv.

FS STEREOSEARCH

DR 549480-07-1

MF C186 H260 Cl4 N12 O28

CI COM

SR CA

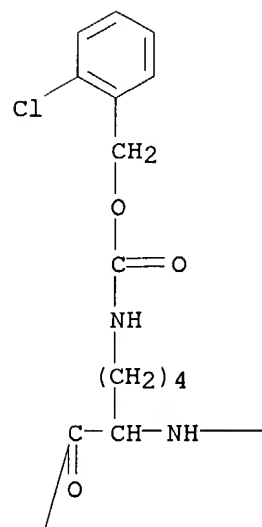
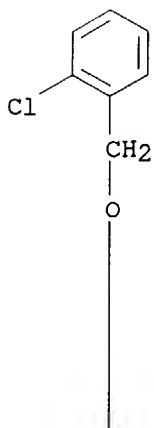
LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Journal

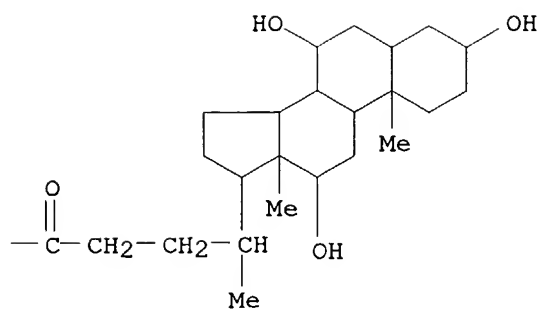
RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties); RACT (Reactant or reagent)

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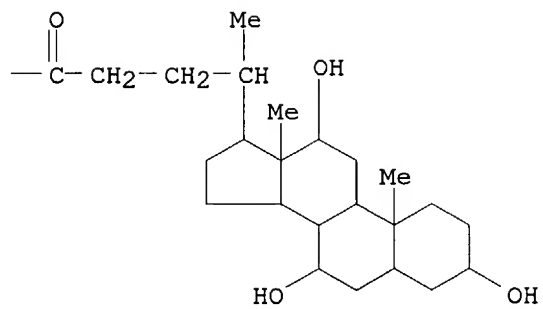
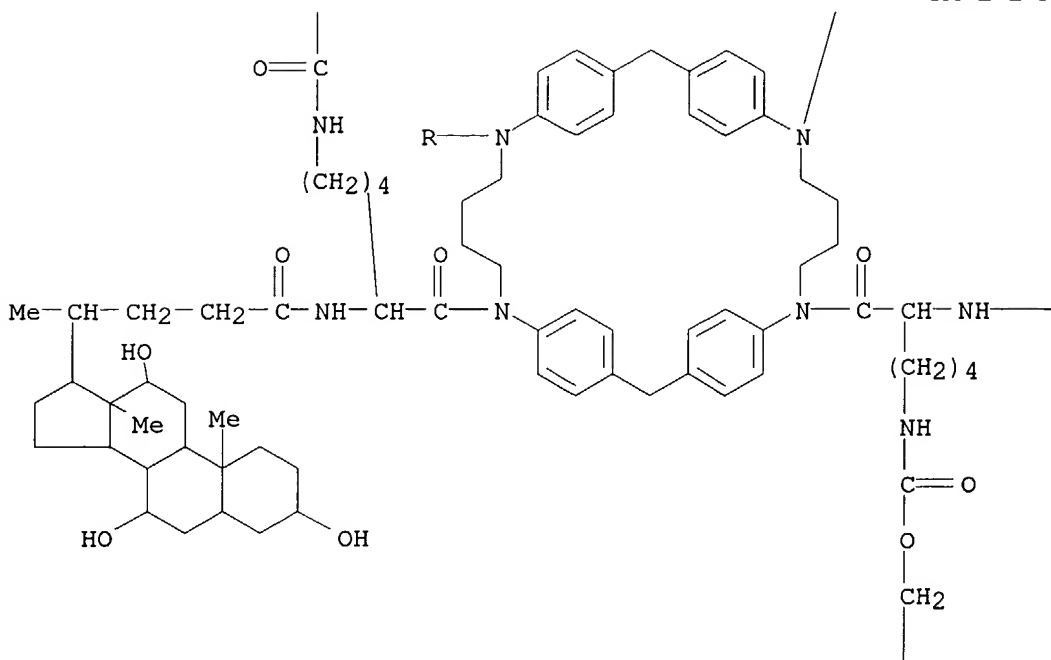
PAGE 1-B



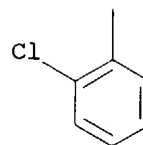
Searcher :

Shears

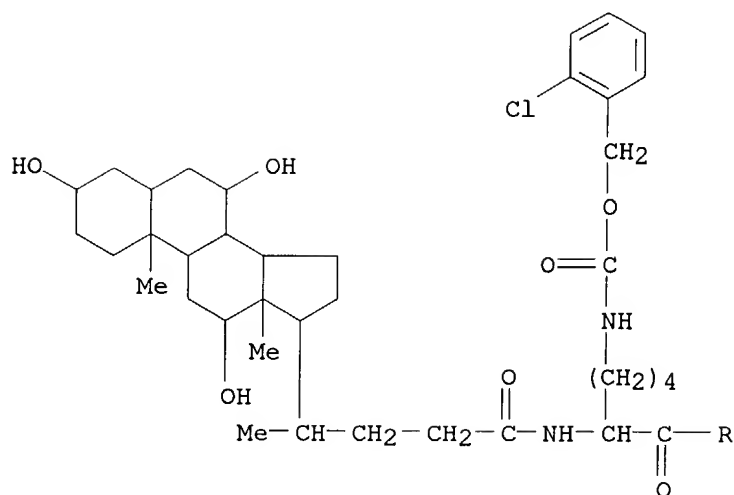
571-272-2528



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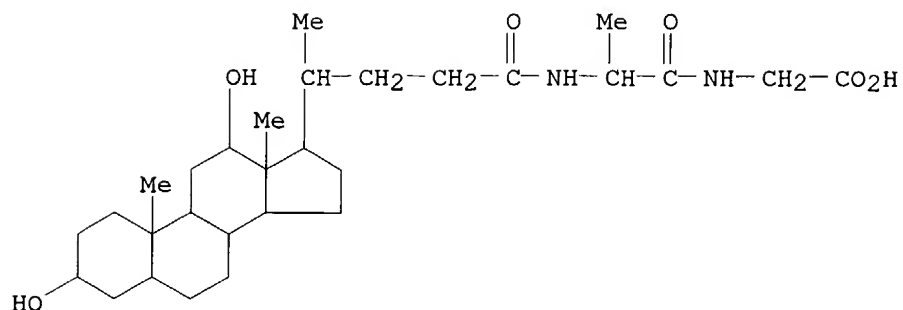
2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 139:68909

REFERENCE 2: 121:102451

L22 ANSWER 50 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 150719-68-9 REGISTRY  
CN Glycine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-L-alanyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, glycine deriv.  
MF C29 H48 N2 O6  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA Caplus document type: Journal  
RL.NP Roles from non-patents: PREP (Preparation)

10/088807

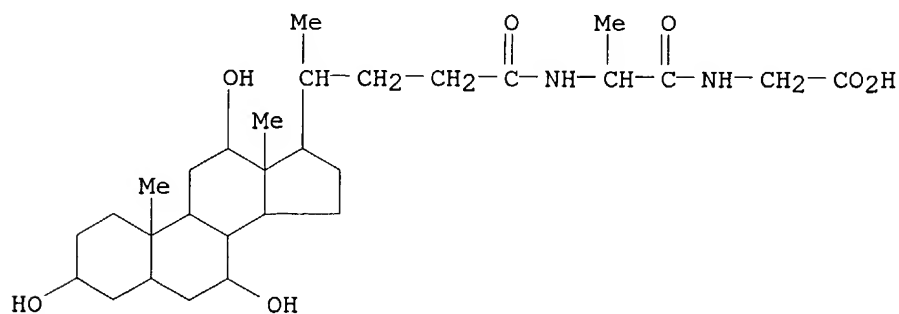


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:210476

L22 ANSWER 51 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN 150698-45-6 REGISTRY  
CN Glycine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-dihydroxy-24-oxocholan-24-yl]-L-alanyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholan, glycine deriv.  
MF C29 H48 N2 O7  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA Caplus document type: Journal  
RL.NP Roles from non-patents: PREP (Preparation)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:210476

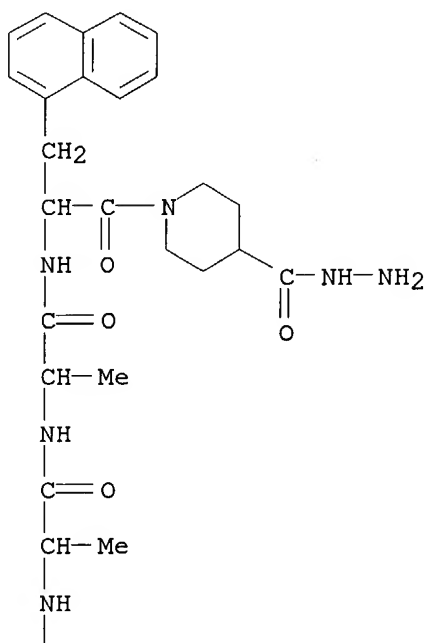
Searcher : Shears 571-272-2528

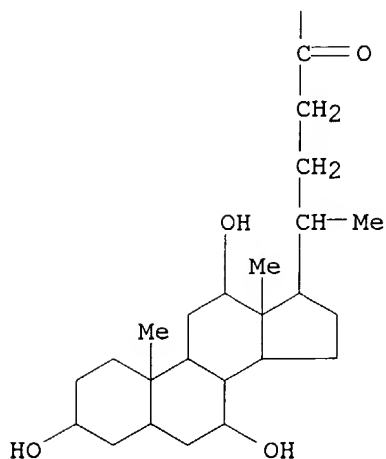
10/088807

L22 ANSWER 52 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **150524-67-7** REGISTRY  
CN L-Alaninamide, N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-alanyl-N-[2-[4-(hydrazinocarbonyl)-1-piperidinyl]-1-(1-naphthalenylmethyl)-2-oxoethyl]-, (S)- (9CI)  
(CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, L-alaninamide deriv.  
FS PROTEIN SEQUENCE  
MF C49 H72 N6 O8  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL  
DT.CA CAPLUS document type: Patent  
RL.P Roles from patents: PREP (Preparation)

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

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1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:203859

L22 ANSWER 54 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **148906-92-7** REGISTRY

CN L-Tyrosine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-3,7-dihydroxy-24-oxocholan-24-yl]-N-methylglycyl]-, ethyl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, L-tyrosine deriv.

MF C38 H58 N2 O7

SR CA

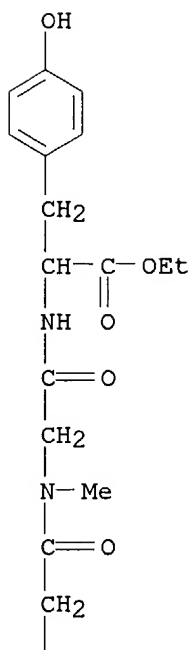
LC STN Files: CA, CAPLUS

DT.CA CAplus document type: Journal

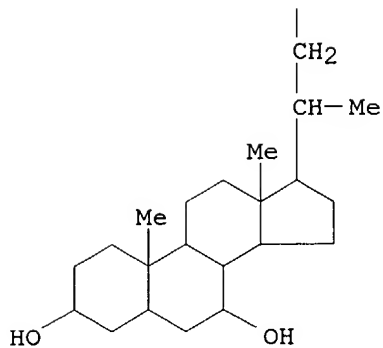
RL.NP Roles from non-patents: PREP (Preparation)

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

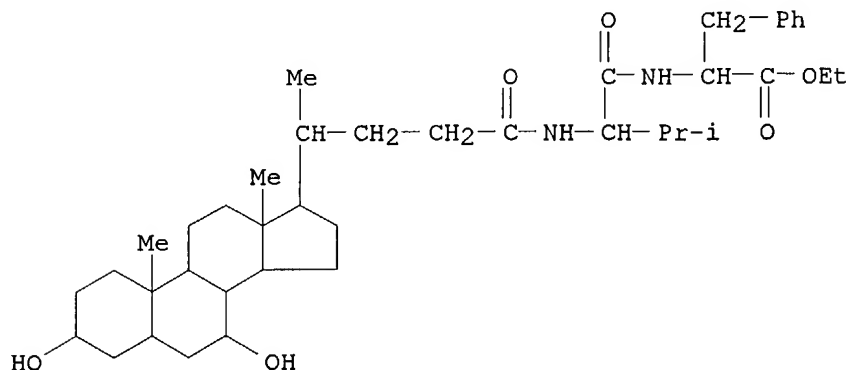
REFERENCE 1: 119:73053

L22 ANSWER 55 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **148893-71-4** REGISTRY  
CN L-Phenylalanine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-3,7-dihydroxy-24-

Searcher : Shears 571-272-2528

10/088807

oxocholan-24-yl]-L-valyl]-, ethyl ester (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, L-phenylalanine deriv.  
MF C40 H62 N2 O6  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA CAplus document type: Journal  
RL.NP Roles from non-patents: PREP (Preparation)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

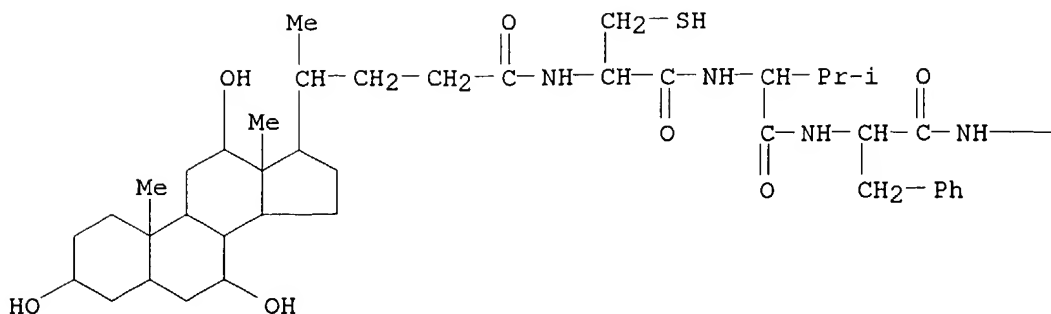
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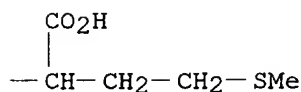
L22 ANSWER 57 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **146296-43-7** REGISTRY  
CN L-Methionine, N-[N-[N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-cysteinyl]-L-valyl]-L-phenylalanyl]- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, L-methionine deriv.  
FS PROTEIN SEQUENCE  
MF C46 H72 N4 O9 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA CAplus document type: Journal; Patent  
RL.P Roles from patents: BIOL (Biological study)  
RL.NP Roles from non-patents: BIOL (Biological study)

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

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2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 121:53129

REFERENCE 2: 118:119560

L22 ANSWER 58 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 134505-87-6 REGISTRY

CN Glycine, N-(24-oxocholan-24-yl)-L-methionyl-L-glutaminyl-L-tryptophyl-L-asparaginyl-L-seryl-L-threonyl-L-alanyl-L-leucyl-L-histidyl-L-glutaminyl-L-alanyl-L-leucyl-L-glutaminyl-L- $\alpha$ -aspartyl-L-prolyl-L-arginyl-L-valyl-L-arginylglycyl-L-leucyl-L-tyrosyl-L-leucyl-L-prolyl-L-alanylglycyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, glycine deriv.

FS PROTEIN SEQUENCE

MF C151 H237 N39 O37 S

SR CA

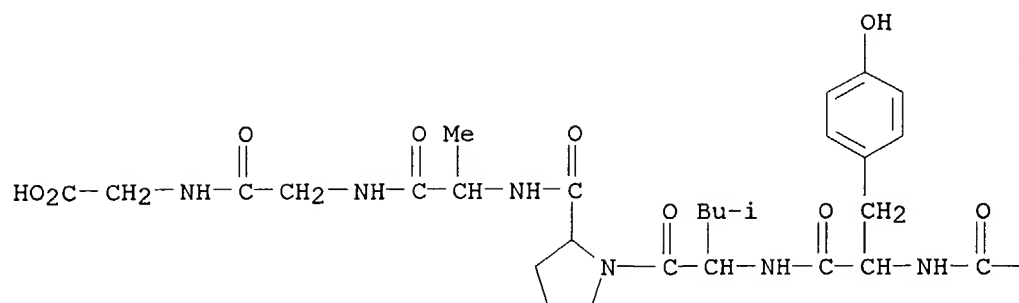
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DT.CA Caplus document type: Journal

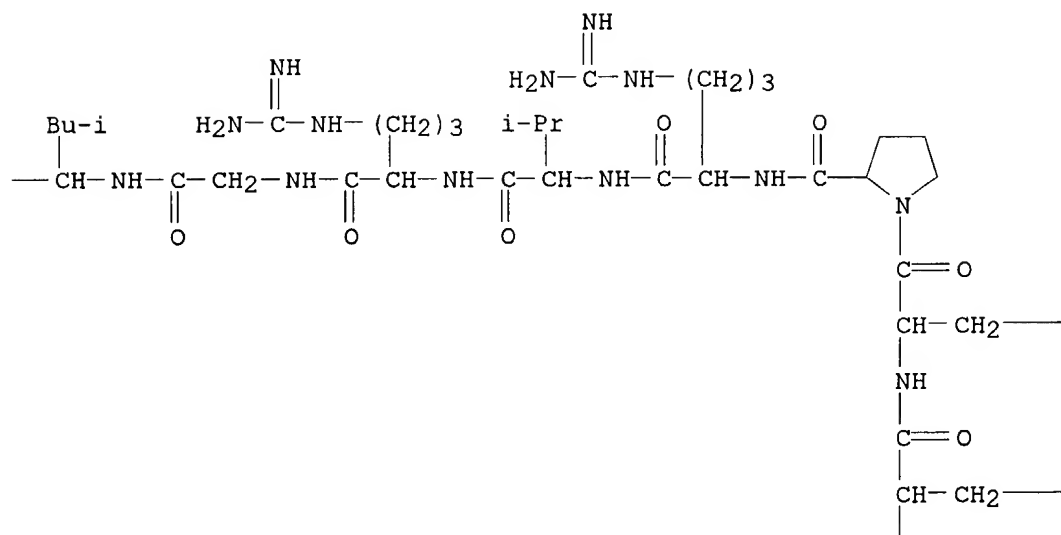
RL.NP Roles from non-patents: BIOL (Biological study); PREP (Preparation); PROC (Process); PRP (Properties)

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*

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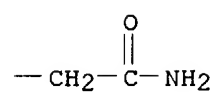
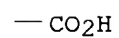


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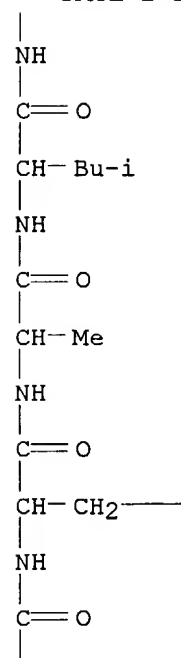


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PAGE 1-C

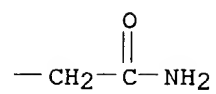


PAGE 2-B

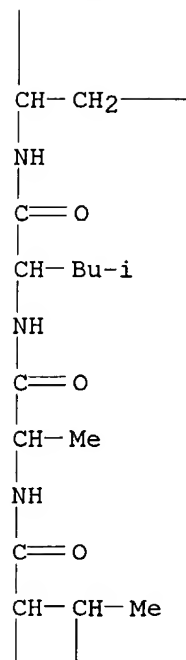


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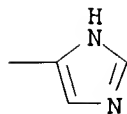


PAGE 3-B

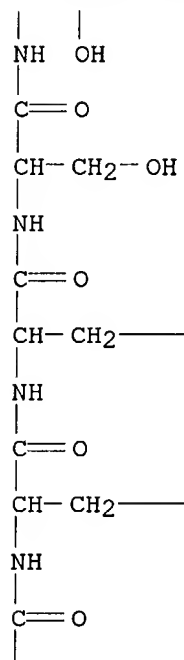


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PAGE 3-C

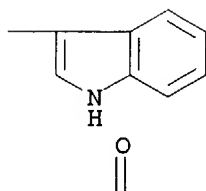
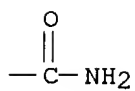


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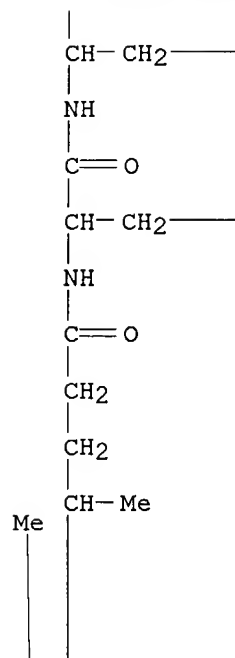


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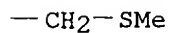
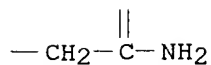
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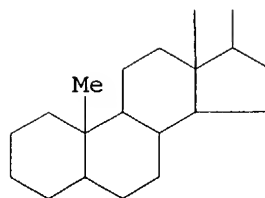
PAGE 5-B



PAGE 5-C



PAGE 6-B



3 REFERENCES IN FILE CA (1907 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 124:286366

REFERENCE 2: 120:71925

REFERENCE 3: 115:29883

L22 ANSWER 59 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **134269-14-0** REGISTRY

CN L-Tyrosine, N-[N-[N2-[N-[N-[N-[1-[N2-[N-[N-(24-oxocholan-24-yl)]-L-cysteiny]]-L-threony]]-L-lysyl]]-L-prolyl]]-L-threony]]-L-α-aspartyl]glycyl]]-L-asparaginy]]-L-cysteiny]]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholan, L-tyrosine deriv.

FS PROTEIN SEQUENCE

MF C68 H106 N12 O18 S2

SR CA

LC STN Files: CA, CAPLUS

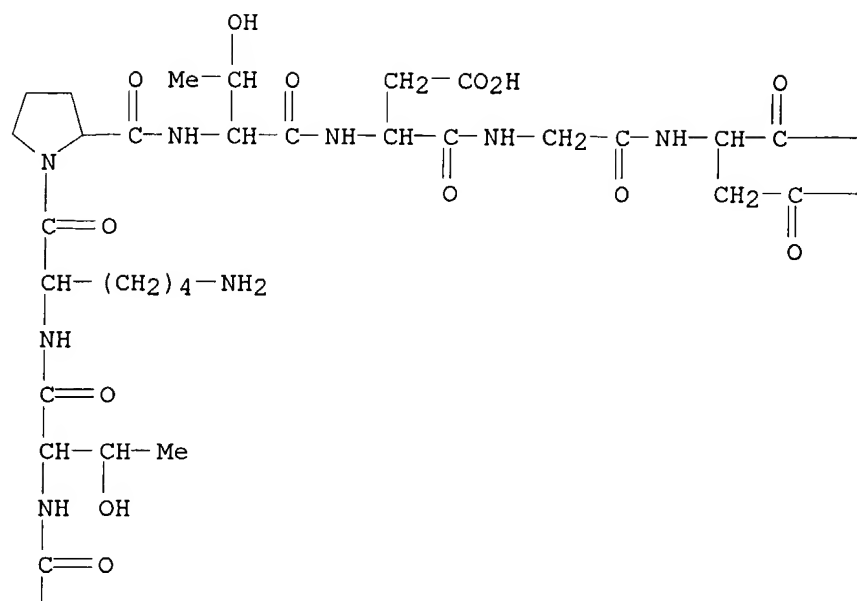
DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: PREP (Preparation); PRP (Properties)

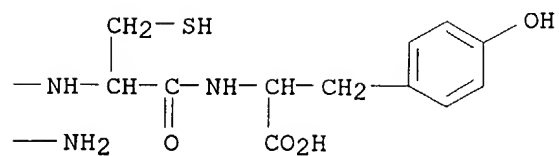
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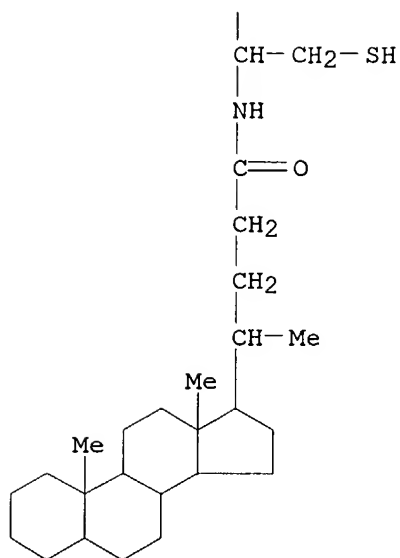
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2 REFERENCES IN FILE CA (1907 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 118:228658

REFERENCE 2: 115:29883

L22 ANSWER 60 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **134009-14-6** REGISTRY

CN Glycine, N-[N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]-L-alanyl]glycyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholan, glycine deriv.

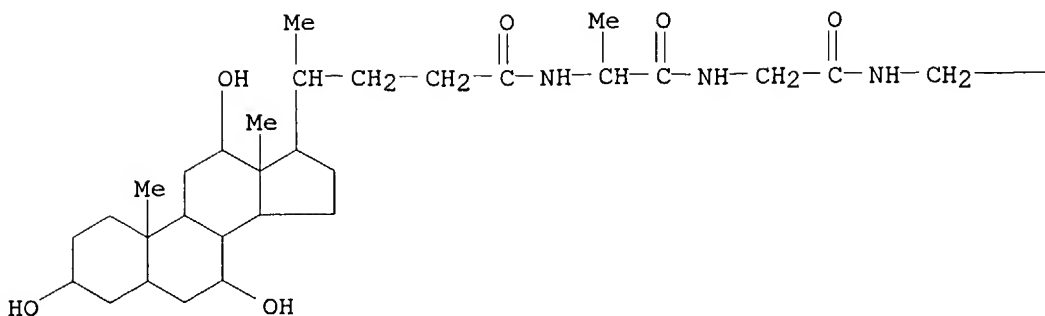
MF C31 H51 N3 O8

SR CA

LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study)

—CO<sub>2</sub>H

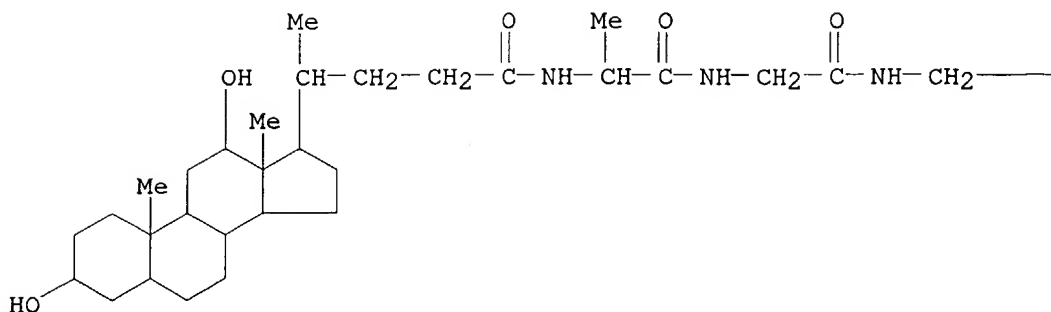
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REFERENCE 1: 114:234930

L22 ANSWER 61 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 133989-67-0 REGISTRY  
 CN Glycine, N-[N-[N-[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]-L-alanyl]glycyl]- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Cholane, glycine deriv.  
 MF C31 H51 N3 O7  
 SR CA  
 LC STN Files: CA, CAPLUS  
 DT.CA Caplus document type: Journal  
 RL.NP Roles from non-patents: BIOL (Biological study)

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PAGE 1-B

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 114:234930

L22 ANSWER 63 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
 RN 125347-56-0 REGISTRY  
 CN Glycine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\beta$ )-3,7-dihydroxy-24-oxocholan-24-yl]glycyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, glycine deriv.

FS STEREOSEARCH

MF C28 H46 N2 O6

SR CA

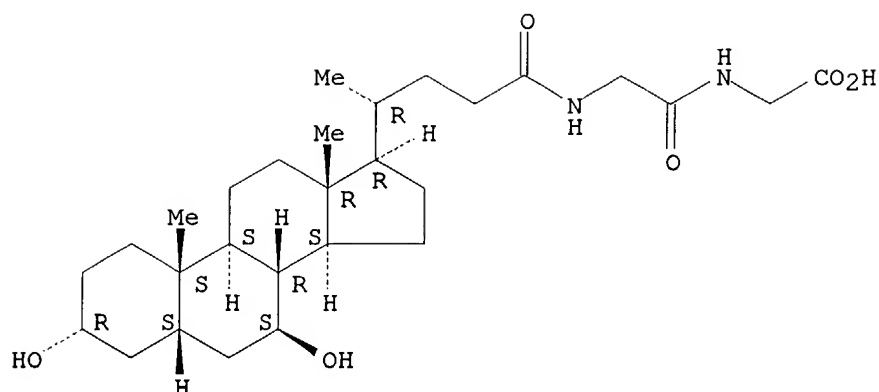
LC STN Files: CA, CAPLUS

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: PREP (Preparation)

Absolute stereochemistry.

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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 112:99233

L22 ANSWER 65 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 121275-23-8 REGISTRY

CN L-Valine, N-[1-[N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ )-3,7-dihydroxy-24-oxocholan-24-yl]-L-alanyl]-L-alanyl]-L-prolyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, L-valine deriv.

FS PROTEIN SEQUENCE

MF C40 H66 N4 O8

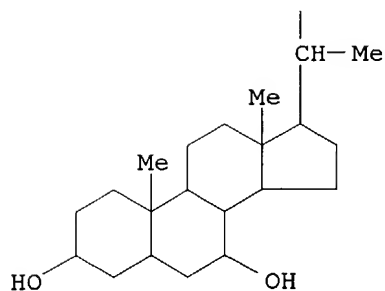
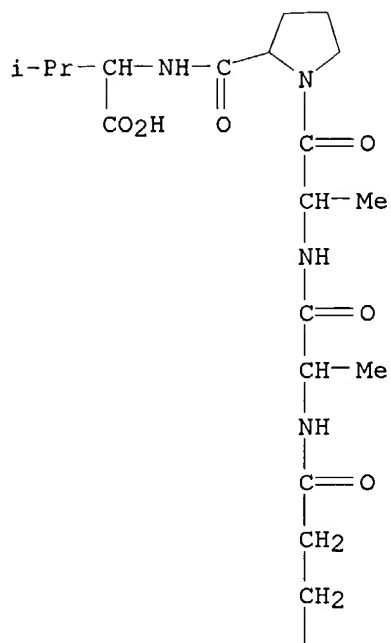
SR CA

LC STN Files: CA, CAPLUS

DT.CA Cplus document type: Journal

RL.NP Roles from non-patents: PREP (Preparation)

\*\*RELATED SEQUENCES AVAILABLE WITH SEQLINK\*\*



1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 111:70314

L22 ANSWER 66 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **115769-72-7** REGISTRY

CN Glycine, N,N-bis(2-chloroethyl)-, (3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ -hydroxy-7,12-dihydroxy-24-oxo-24-[[2-oxo-2-(phenylmethoxy)ethyl]amino]cholan-3-yl ester (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, glycine deriv.

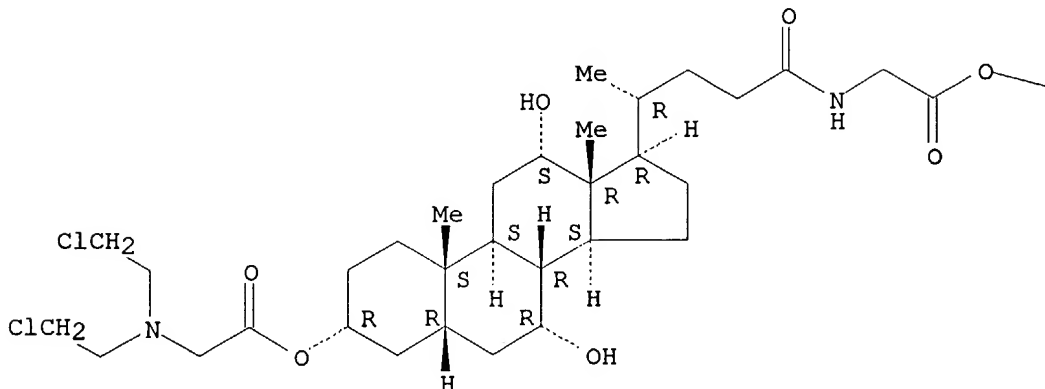
FS STEREOSEARCH

10/088807

MF C39 H58 Cl2 N2 O7  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL  
DT.CA Caplus document type: Patent  
RL.P Roles from patents: PREP (Preparation)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



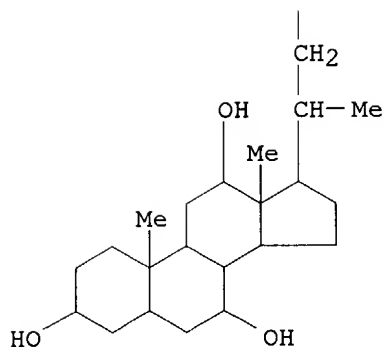
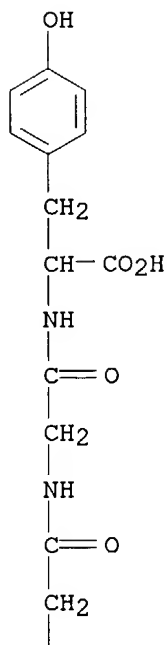
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 109:93443

L22 ANSWER 67 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN  
RN **111933-30-3** REGISTRY  
CN L-Tyrosine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-  
trihydroxy-24-oxocholan-24-yl]glycyl]-, labeled with carbon-14 (9CI)  
(CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Cholane, L-tyrosine deriv.  
MF C35 H52 N2 O8  
SR CA  
LC STN Files: CA, CAPLUS  
DT.CA Caplus document type: Journal  
RL.NP Roles from non-patents: PREP (Preparation)  
IL XC-14

Searcher :       Shears       571-272-2528



1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 108:19604

L22 ANSWER 68 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **108147-75-7** REGISTRY

CN L-Tyrosine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,5,7,12-tetrahydroxy-24-oxocholan-24-yl]glycyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

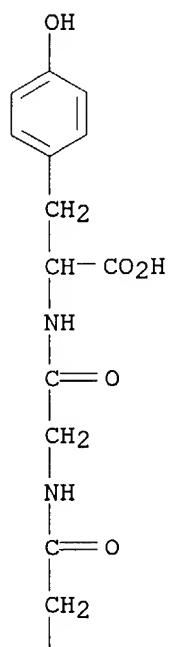
CN Cholane, L-tyrosine deriv.

MF C35 H52 N2 O9

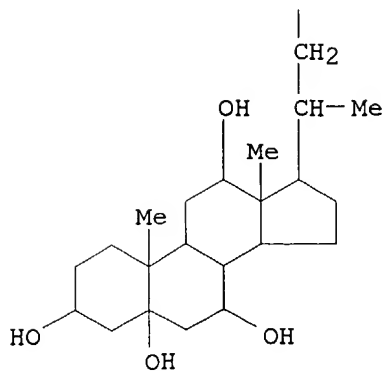
10/088807

SR CA  
LC STN Files: CA, CAPLUS  
DT.CA CAplus document type: Journal  
RL.NP Roles from non-patents: BIOL (Biological study)

PAGE 1-A



PAGE 2-A



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

Searcher : Shears 571-272-2528

10/088807

REFERENCE 1: 106:193422

L22 ANSWER 69 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **103528-73-0** REGISTRY

CN Glycine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )-3,12-dihydroxy-24-oxocholan-24-yl]glycyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, glycine deriv.

FS STEREOSEARCH

MF C28 H46 N2 O6

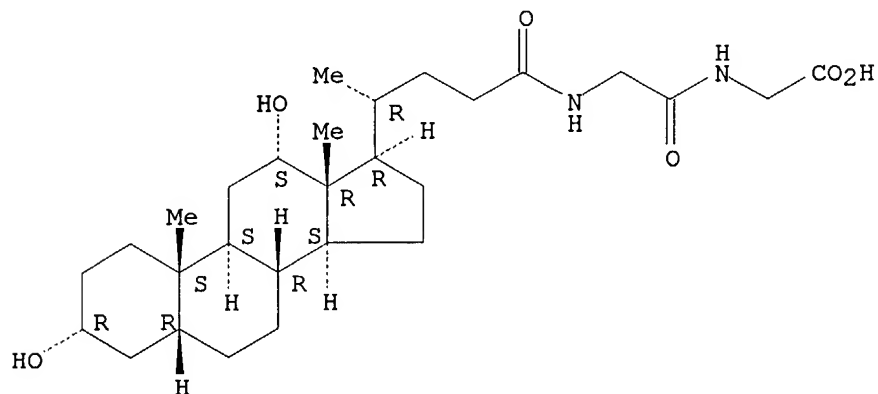
SR CA

LC STN Files: CA, CAPLUS

DT.CA Caplus document type: Journal

RL.NP Roles from non-patents: PREP (Preparation); RACT (Reactant or reagent)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1907 TO DATE)

2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 119:210476

REFERENCE 2: 105:76527

L22 ANSWER 76 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **98584-72-6** REGISTRY

CN Glycine, N-[N-[N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]glycyl]glycyl]glycyl]- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Cholane, glycine deriv.

OTHER NAMES:

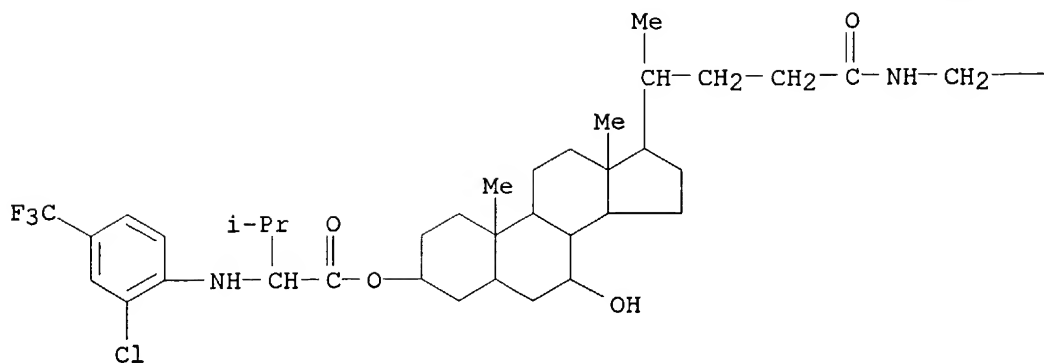
CN Cholyltetraglycine

FS PROTEIN SEQUENCE; STEREOSEARCH

MF C32 H52 N4 O9

Searcher : Shears 571-272-2528



— CO<sub>2</sub>H

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 97:105275

L22 ANSWER 83 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **82186-93-4** REGISTRY

CN Valine, N-[2-chloro-4-(trifluoromethyl)phenyl]-, 3-ester with  
 N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-  
 oxocholan-24-yl]glycine (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

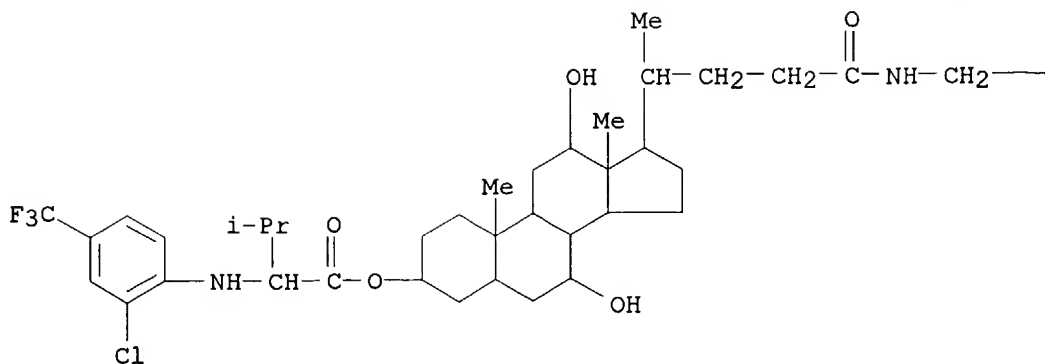
CN Cholane, DL-valine deriv.

MF C38 H54 Cl F3 N2 O7

LC STN Files: CA, CAPLUS, TOXCENTER

DT.CA CAplus document type: Journal

RL.NP Roles from non-patents: BIOL (Biological study)

—CO<sub>2</sub>H

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1907 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 97:105275

L22 ANSWER 84 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN 76763-11-6 REGISTRY

CN L-Tyrosine, 3-(iodo-125I)-N-[[[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-  
 3,7,12-trihydroxy-24-oxocholan-24-yl]amino]acetyl]- (9CI) (CA INDEX  
 NAME)

OTHER CA INDEX NAMES:

CN Choline, L-tyrosine deriv.

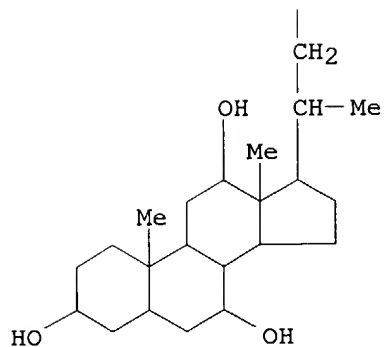
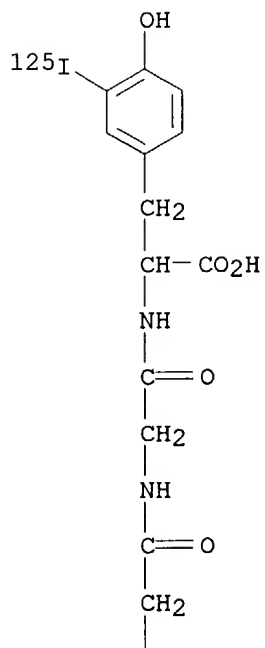
MF C35 H51 I N2 O8

LC STN Files: CA, CAPLUS, USPATFULL

DT.CA Caplus document type: Journal; Patent

RL.P Roles from patents: PREP (Preparation)

RL.NP Roles from non-patents: PREP (Preparation)



2 REFERENCES IN FILE CA (1907 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 100:100527

REFERENCE 2: 94:103833

L22 ANSWER 85 OF 98 REGISTRY COPYRIGHT 2004 ACS on STN

RN **74427-77-3** REGISTRY

CN L-Tyrosine, N-[N-[(3 $\alpha$ ,5 $\beta$ ,7 $\alpha$ ,12 $\alpha$ )-3,7,12-trihydroxy-24-oxocholan-24-yl]glycyl]-, methyl ester (9CI) (CA